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THE MECHANISM OF AURICULAR PAROXYSMAL TACHYCARDIA

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AURICULAR paroxysmal tachycardia was long ago described and recognized as a clinical entity, but the fundamental mechanism or mechanisms responsible for this disorder have not yet been finally ascertained.[1, 2] Unlike auricular flutter and auricular fibrillation, it cannot be readily induced in experimental animals, and cannot, therefore, be easily studied by this method. Speculations as to its nature must, therefore, be based on pertinent observations on man. We propose to discuss from this standpoint the following features of this disturbance: (1) the form of the auricular deflections; (2) the effects of exertion, vagal stimulation, digitalis, quinidine, and other drugs upon the auricular rate and the duration of the paroxysms; (3) similarities, differences, and relations between it and auricular flutter and fibrillation; (4) the spontaneous occurrence of auriculoventricular block in a small number of cases and the difficulty or impossibility of producing it in most of the others; and (5) the occurrence of alternation in the auricular cycle length. We wish particularly to examine the suggestion[3] that auricular paroxysmal tachycardia is caused by circus rhythm involving one of the specialized auricular nodes.

When Mines[4] described circus rhythm he suggested that it might be responsible for some cases of paroxysmal tachycardia in man. Iliescu and Sebastiani[5] were among the first to suggest that auricular paroxysmal tachycardia is due to circus contraction. Their reasoning was based chiefly on the action of quinidine in this disorder. Lewis[2] pointed out that the total amount of auricular muscle is not sufficiently large to accommodate a circus mechanism at known rates of conduction in auricular

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muscle and with cycles as long as those which occur in auricular paroxysmal tachycardia. For this reason and because of the isoelectric intervals separating the auricular deflections, he could not accept circus rhythm as the cause of this disorder. He did not mention the possibility that the path of the circus impulse might pass through one of the specialized auricular nodes. Ashman and Hull[3] have suggested that in auricular paroxysmal tachycardia there is a circus rhythm in which the re-entrant impulse passes through one of the nodes. In a necessarily brief discussion they presented only a part of the evidence which supports this view. They mentioned especially the effects of vagal stimulation and the slowness of the rate, as compared with auricular flutter, in relation to the slowness of conduction through nodal tissue.

The Form of the Auricular Deflections.—The form of the auricular deflections was examined in the electrocardiograms of one hundred unselected cases of auricular paroxysmal tachycardia. In thirty-four they were upright in Leads I and II, and in many of these the P waves closely resembled, or were identical with, those recorded when normal sinus rhythm was present. In fourteen cases the auricular deflections were inverted in Leads II and III. In fifty cases these deflections were intermediate in form, very small, flat or diphasic, or they were not clearly visible because they were small and superimposed upon some part of the ventricular complex. In many of the cases in which there were upright P waves the impulse must have entered the main mass of auricular muscle near the normal pacemaker in the upper part of the sinoauricular node. The inverted P waves suggest beats arising in or near the auriculoventricular node, or in some outlying part of the auricular muscle. The point of origin of beats represented by auricular deflections of intermediate form cannot be stated with certainty. Lewis[2, 6] has shown that deflections of this form may arise in a region between the upper part of the sinoauricular node and the auriculoventricular node, and that they may be produced by impulses arising in the lower part of the sinoauricular node. With two exceptions the form of the auricular deflections in the cases of auricular paroxysmal tachycardia which we reviewed is not inconsistent with the view that the paroxysmal focus lay in or near the sinoauricular node or in or near the auriculoventricular node. The exceptions were two cases in which the auricular deflections were inverted in Lead I and upright in Leads II and III. Such cases are very uncommon; in them the form of the auricular deflections suggests a focus located in the upper part of the left atrium.

The Stability of the Rate.—In auricular paroxysmal tachycardia the auricular rate is ordinarily remarkably constant. It is not, as a rule, influenced by rest, posture, emotion, or exertion. It is not under the control of the extrinsic cardiac nerves, as are slower rhythms of the normal type arising in the sinoauricular node or the auriculoventricular node. Even at the onset of attacks, and at the end of paroxysms terminating

spontaneously, there is usually little or no alteration of the rate. The patients with upright auricular deflections in Leads I and II, and especially those with atrioventricular block, show somewhat more variation in auricular rate than do those whose auricular waves are inverted or intermediate in form, with no block.

Exercise.—The auricular rate in auricular paroxysmal tachycardia is sometimes increased by exercise,[7*, 8] but in auricular fibrillation the opposite is usually observed.[9†] Slowing of the fibrillating auricles on exertion is attributed to a reduction of vagal tone; atropine also slows the rate of the fibrillating auricles.[11] The acidosis accompanying exercise should, by depressing conduction in the auricles, tend further to reduce their rate.[4, 12, 13] The occasional increase in the rate of auricular paroxysmal tachycardia on effort may be attributed to a reduction of vagal tone; acidosis should cause slowing, whatever the mechanism.

Stimulation of the Vagus.—In auricular paroxysmal tachycardia, pressure upon the carotid sinus and other measures which stimulate the vagus nerves not uncommonly slow the rate of the paroxysm and frequently restore normal rhythm.[14, 15] As a rule the slowing occurs immediately preceding the termination of the attack, but occasionally the rate is slowed when the attack is not stopped.

Vagal stimulation diminishes the rate of impulse production in the sinoauricular and the auriculoventricular node, and depresses conduction in the latter. Its effect upon the rate of conduction in the sinoauricular node and upon the rate of impulse production in auricular muscle outside the nodes is not known. Vagal stimulation shortens the effective refractory period of ordinary auricular muscle and improves its conductivity. In disorders caused by circus rhythm in auricular muscle these effects tend to increase the number of cycles per minute.[16] The slowing of the rate of paroxysmal tachycardia and the restoration of normal rhythm by vagal stimulation cannot be explained by the effect of increased vagal tone upon the characteristics of the ordinary auricular muscle, and are most logically attributed to the action of these nerves upon the nodes.

Digitalis.—Like vagal stimulation, digitalis often slows the rate of auricular paroxysmal tachycardia and restores normal rhythm.[17] Occasionally the drug slows the rate without stopping the tachycardia, but usually the slowing occurs only a short time before the termination of the attack. Digitalis acts directly upon the heart muscle, and indirectly by stimulating the vagus nerves. In auricular fibrillation and flutter the increase in the circus rate produced by the drug is apparently caused primarily by increased vagal tone, which shortens the refractory period of the ordinary auricular muscle. The slowing of the ventricular rate

*Case 9.

†Doumer[10] has observed in auricular flutter an increase in auricular rate after exercise. This is exceptional.

is due to both a direct and an indirect depression of the conductivity of the atrioventricular node. The effects of digitalis in paroxysmal auricular tachycardia cannot be attributed to shortening of the refractory period of the auricular muscle, and would seem to depend upon its nodal action or upon some effect as yet unknown. The effect of digitalis upon conduction within the sinoauricular node is not known. The direct action of the drug upon auricular muscle is to increase its effective refractory period and to depress its conductivity.[18, 19] This effect can scarcely account for its ability to slow or abolish auricular paroxysmal tachycardia; it is opposed by the indirect vagal action of the drug upon the auricular muscle, and the effects of digitalization and vagal stimulation in the condition are similar, not opposite. The effect of the drug upon the rate of impulse production in auricular muscle outside the nodes is not known. If the slowing of the rate and the restoration of normal rhythm in auricular paroxysmal tachycardia are caused by any of the known effects of this drug, it would seem that they must be attributed to its effects upon nodal tissue.

Quinidine.—Quinidine and quinine likewise often slow the rate of auricular paroxysmal tachycardia and sometimes restore normal rhythm.[5, 8, 20] These drugs, too, act upon the heart both directly and indirectly. The indirect effect is a reduction of vagal tone. In the auriculoventricular node the direct and vagal actions are opposed; the direct effect is to depress conduction and the indirect to improve it. Consequently, the changes in auriculoventricular conductivity are somewhat variable.[21] In auricular muscle both the direct and the indirect actions increase the effective refractory period and depress conductivity. It is through these effects that these drugs invariably slow the circus rate and often restore normal rhythm in auricular fibrillation and flutter.[19, 21, 22] In man they do not slow the rate of simple sinus tachycardia;[20, 23] indeed, they often increase the rate of slower sinus rhythm.[20] In dogs both acceleration and slowing of the sinus rhythm have been observed under different conditions.[21, 24, 25] It is difficult to understand how the known effects of these drugs upon conductivity and upon the effective refractory period can bring about slowing of the rate and restoration of normal rhythm in abnormal tachycardias not caused by circus rhythm.

Relation to Auricular Flutter and Fibrillation.—Auricular paroxysmal tachycardia sometimes changes spontaneously to auricular flutter or fibrillation, or flutter or fibrillation may change to paroxysmal tachycardia.[26, 27, 28] In some cases digitalis may have converted paroxysmal tachycardia into fibrillation.[7, 29] Such changes in rhythm, although not common, suggest a relationship between these disorders.

In the preceding paragraphs mention has been made of some of the similarities and differences between auricular paroxysmal tachycardia, on the one hand, and auricular flutter and fibrillation, on the other, with respect to the effects of exertion, vagal stimulation, digitalis, and

quinidine. Like paroxysmal flutter and fibrillation, auricular paroxysmal tachycardia begins and ends abruptly. The auricular rate in paroxysmal tachycardia, as in flutter and fibrillation, is quite stable; it is not often influenced appreciably by rest, posture, emotion, or exercise, as is the normal sinus rhythm. Auricular paroxysmal tachycardia with partial auriculoventricular block resembles auricular flutter in many respects.[7, 30] Quinidine usually slows the heart rate in paroxysmal tachycardia, and always slows the circus rate in fibrillation and flutter, but does not slow sinus tachycardia. These features of auricular paroxysmal tachycardia suggest that its mechanism, like that of flutter and fibrillation, may depend on circus rhythm.

The mechanism of auricular paroxysmal tachycardia cannot, however, be a circus contraction involving ordinary auricular muscle only, like that of auricular flutter or fibrillation. In some instances exercise increases the rate of auricular paroxysmal tachycardia, but it usually slows the rate of the fibrillating auricles. Vagal stimulation and digitalis often slow the rate of paroxysmal tachycardia, whereas, in flutter and fibrillation, they increase the circus rate. Furthermore, as pointed out by Lewis,[2] the total amount of auricular muscle is not sufficiently large to accommodate a circus mechanism at known rates of conduction and with cycles as long as those of auricular paroxysmal tachycardia. In addition, the auricular deflections of paroxysmal tachycardia, unlike those of flutter, are separated by intervals of electrical quiescence, in which the galvanometer string is at rest in the isoelectric position.[2, 7, 31]

The separation of the auricular deflections of paroxysmal tachycardia by isoelectric intervals is shown commonly in standard leads, usually in chest leads, and always in esophageal leads; it is most clearly seen in cases of tachycardia with auriculoventricular block in those auricular cycles which are entirely free of ventricular deflections.[7, 31] This is quite different from flutter, in which the electrocardiographic oscillations are continuous; the tracing never comes completely to rest at the isoelectric line. Complete separation of the auricular deflections is inconsistent with circus rhythm unless some way is found to account adequately for isoelectric intervals during the continuous activity of the circus movement. They could be accounted for if the circus path traversed either the sinoauricular or the auriculoventricular node. While the advancing wave of activity was passing through the node, the amount of tissue entering the active state would be too small to produce electrical forces detectable by present methods. The observed auricular deflection would be inscribed by the activation of auricular muscle after the impulse emerged from the node. Its form and direction would be governed by the point at which the impulse entered the main body of the auricular muscle. Impulses emerging from the upper part of the sinoauricular node should give rise to upright deflections not unlike those of normal rhythm, impulses emerging from the atrioventricular

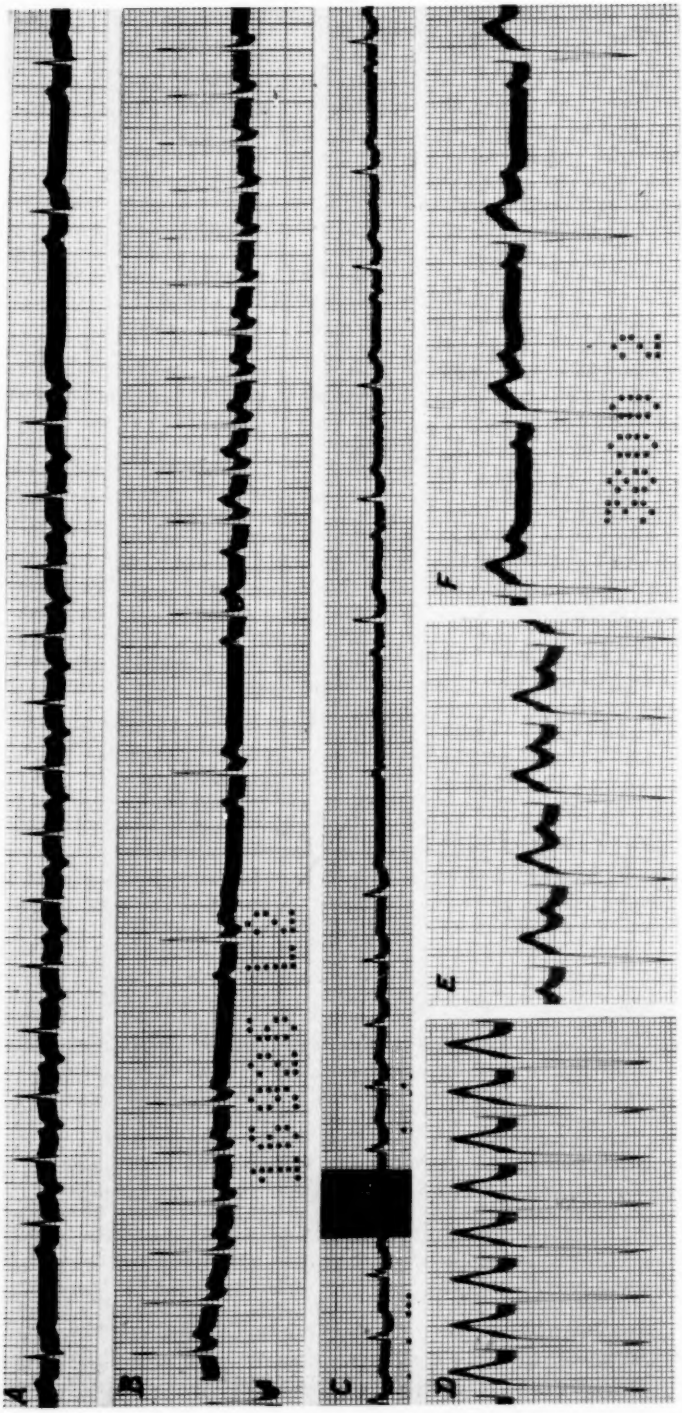

Fig. 1.—Electrocardiograms illustrating the relationship between the termination of attacks of auricular paroxysmal tachycardia and depression of atrioventricular conductivity. *A*, Lead II: a paroxysm ends spontaneously with an abnormal auricular beat which is blocked. *B*, Lead II: deep breathing; the P-R interval is prolonged (0.28 second) after the first normal auricular beat, and somewhat shorter (0.24 to 0.22 second) in subsequent beats. *C*, Lead II: pressure upon the carotid sinus; the first normal auricular beat is blocked. *D*, *E*, and *F*, chest leads; the paroxysm (*D*) was stopped by digitalis; normal rhythm (*E*) was followed almost immediately by 2 to 1 atrioventricular block (*F*).

node should give rise to inverted deflections like those of atrioventricular rhythm, and deflections of intermediate form might be produced by impulses emerging from the lower part of the sinoauricular node.[2, 6] In a mechanism such as this a circus rhythm could be accommodated in auricular muscle and in one of the specialized nodes at known rates of conduction and with cycle lengths such as occur in auricular paroxysmal tachycardia. The rate of the tachycardia would depend chiefly upon the speed of conduction and the length of the path within the nodal tissue.

Auriculoventricular Block.—Auriculoventricular block is extremely rare in those cases in which inversion of the auricular deflections suggests that the paroxysmal focus lies in or near the auriculoventricular node. It seems strange, in view of the high auricular rate, that block should occur so rarely. The most reasonable explanation would seem to be that the agents which tend to produce block, namely, vagal stimulation and digitalis, terminate the paroxysm before block occurs. It is easy to understand that this might happen in tachycardia which is dependent upon circus rhythm involving the atrioventricular node. At any rate, it appears that, in many cases of this kind, unimpaired conduction in this node is essential to maintenance of the paroxysmal tachycardia, and that depression of conduction in this node is intimately related to the termination of the attacks.

Not infrequently this relationship is apparent when the end of the paroxysm is recorded; sometimes the last paroxysmal auricular impulse is blocked, or block appears immediately after the cessation of the attack. Several electrocardiograms illustrating this phenomenon are shown in Fig. 1. Curve *A* (Lead II) shows a short attack of auricular paroxysmal tachycardia in its entirety. It begins with a premature inverted auricular deflection which resembles an auricular extrasystole, and ends spontaneously with a similar beat which is blocked. The P-R interval is slightly prolonged (0.24 second), both during the normal and during the abnormal rhythm. The last four cycles of the paroxysm are longer than those that precede them. A somewhat more complicated disturbance is shown in Curve *B;* in this case, deep breathing temporarily stopped an attack of auricular paroxysmal tachycardia. During the paroxysm the P-R interval was prolonged and the inverted auricular deflections (Lead II) followed closely the R waves of the preceding beats. The attack ended with a blocked auricular beat. The first and second beats after the end of the paroxysm are complicated by blocked auricular extrasystoles, as shown by the inverted auricular deflections which closely follow the R waves. The third beat is not so disturbed, but the fourth beat is followed immediately by a similar premature auricular beat which initiates another paroxysm of tachycardia. The P-R interval is abnormally long (0.28 second) after the first normal auricular beat, and somewhat shorter (0.24 to 0.22 second) in subsequent beats—the patient had received digitalis. In a third patient (Tracing

C) pressure upon the carotid sinus stopped the paroxysm. The auricular deflections (Lead II) are not clearly visible during the tachycardia. The first normal auricular beat is blocked, and subsequently the P-R interval is prolonged (0.25 to 0.27 second). In a fourth case the paroxysm (Curve *D*) was stopped by a large dose of digitalis given intravenously; the onset of normal rhythm (Curve *E*) was followed almost immediately by 2 to 1 atrioventricular block (Curve *F*). These last curves were obtained by means of a chest lead.

Partial auriculoventricular block occurs spontaneously in a few patients with auricular paroxysmal tachycardia, and it can be induced by vagal stimulation, or by digitalis, in a few others. In the great majority of all the cases in which block is present or can be induced, the P waves are similar in form to those recorded when normal sinus rhythm is present.[7] It is conceivable that in such cases the tachycardia is caused by circus rhythm involving the sinoauricular node, and that agents which tend to induce atrioventricular block do not depress conductivity within the sinoauricular node sufficiently to block the circus path. The auricular rate appears to be notably more variable in this group of cases than in those in which block cannot be induced.

It should be pointed out, however, that block cannot be induced in many cases in which the form of the P wave suggests that the paroxysmal focus lies in or near the sinoauricular node, and also that it occasionally occurs or can be induced in cases in which the form of the P waves suggests that the paroxysmal focus lies in or near the atrioventricular node.

Alternation of Cycle Length.—In a small proportion of cases of auricular paroxysmal tachycardia there occurs a slight irregularity characterized by alternation of relatively long and relatively short auricular cycles.[32] This has been observed in auricular flutter, also.[33] This phenomenon can be explained most satisfactorily by assuming that the mechanism of auricular paroxysmal tachycardia is circus rhythm.[32]

DISCUSSION

The various features of auricular paroxysmal tachycardia which have been discussed suggest that (1) the specialized nodes are involved in its mechanism, (2) the abnormal mechanism is circus rhythm, and (3) the circus rhythm is of a special kind. That the specialized nodes participate in the abnormal mechanism is suggested by (1) the form of the auricular deflections, (2) the acceleration of the auricular rate by exercise, (3) the slowing of the auricular rate and the termination of attacks by vagal stimulation and by digitalis, and (4) the rarity of atrioventricular block, especially in paroxysms arising in the region of the auriculoventricular node. That the mechanism of the disorder is circus rhythm is suggested by (1) the abrupt onset and termination of attacks, (2) the remarkable stability of the rate, (3) the slowing of the auricular rate and the termination of paroxysms by quinidine, and (4) the occasional alternation of

cycle length. That the circus rhythm is of a special kind is indicated by (1) the slowing of the auricular rate and the termination of attacks by vagal stimulation and by digitalis, (2) the acceleration of the auricular rate by exercise, (3) the relatively slow rate and long cycle length, and (4) the separation of the auricular deflections by isoelectric intervals.

A circus rhythm involving in its path one of the specialized auricular nodes most adequately accounts for these features of auricular paroxysmal tachycardia. No one of them is of itself decisive, but all together point strongly toward this mechanism. It accounts most satisfactorily for the abrupt onset and termination of the paroxysms, the stability of the rate, the form of the auricular deflections and their separation by isoelectric intervals, the relatively slow rate and long cycle length, the rarity of atrioventricular block and the impossibility of producing it in most cases, the acceleration of the rate by exercise, and the slowing of the rate and termination of attacks by vagal stimulation, digitalis, and quinidine.

It is necessary, however, to consider several exceptions which cannot readily be explained in this manner. One exception is represented by the rare cases which resemble paroxysmal tachycardia but in which the rate slows gradually to normal.[34, 35] In these cases the auricular deflections are identical with those which occur during normal sinus rhythm. They are probably not examples of true auricular paroxysmal tachycardia of the type under discussion, but rather of an unusual and persistent type of sinus tachycardia. Another apparent inconsistency is represented by those rare cases of auricular paroxysmal tachycardia in which there are auricular deflections of varying form.[7,* 27, 36, 37] They suggest that the impulses originate in two different regions of the auricles. The explanation for this is not apparent. If the mechanism in these cases is circus rhythm, the circus path in the auricles must change markedly, or there must be two different regions of circus activity. A third exception is represented by the cases in which the auricular deflections are inverted in Lead I and upward in Leads II and III. The form of the deflections suggests that they arise in the upper part of the left atrium, far from the nodes of specialized tissue. Such cases are decidedly uncommon; there were only two among our one hundred unselected cases. All of these exceptions are rare, and need not influence our main conclusions.

In the light of the available evidence, which, if not conclusive, is at least very strong, we suggest that the view that auricular paroxysmal tachycardia is caused by circus rhythm involving one of the specialized nodes—the sinoauricular or the auriculoventricular node—deserves serious consideration.

*Case 15.

SUMMARY AND CONCLUSIONS

1. Many of the important features of auricular paroxysmal tachycardia have been considered from the standpoint of their significance in elucidating the mechanism underlying this disorder.

2. The slowing of the auricular rate and the termination of the paroxysms by vagal stimulation and by digitalis and the acceleration of the rate by exercise suggest that the abnormal mechanism is influenced by the action of these agents upon one of the specialized auricular nodes.

3. The form of the auricular deflections indicates that they originate in or near these nodes.

4. The extreme rarity of atrioventricular block in cases in which there are inverted auricular deflections suggests that in these cases the auriculoventricular node is involved in the abnormal mechanism.

5. The abrupt onset and termination of the attacks, the remarkable stability of the rate, the slowing of the auricular rate and the termination of the attacks by quinidine, and the occasional alternation in cycle length suggest that the abnormal mechanism is circus rhythm.

6. The slowing of the auricular rate and the termination of the attacks by vagal stimulation and by digitalis, the acceleration of the rate by exercise, the relatively slow rate and long cycle length, and the separation of the auricular deflections by isoelectric intervals suggest that the circus rhythm is of a special kind.

7. No one of the above features is of itself decisive, but all together point strongly toward circus rhythm in the auricles, the path of which passes through one of the specialized auricular nodes, as the underlying mechanism of auricular paroxysmal tachycardia. This mechanism accounts most satisfactorily for all of the above features.

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PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA WITH A-V BLOCK

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THEORETICALLY, extremely rapid heart action would be expected to produce fatigue and block in the conduction pathways rather frequently. Atrioventricular block in the presence of paroxysmal tachycardia is generally considered uncommon. Our experiences have led us to believe, however, that the occurrence is much more frequent than heretofore suspected.

A survey of the literature on cases of paroxysmal supraventricular tachycardia in which the diagnosis was confirmed by electrocardiographic studies would lead to the conclusion that atrioventricular block is only occasionally recorded during paroxysms of atrial tachycardia. There is a paucity of reports of such cases; after Lewis'[1] original observation, in 1909, it was fifteen years before the next case was put on record by Drury,[2] in 1924. The paper by Sprague and White,[3] in 1925, seems to be the only study directed toward determining the frequency of this condition. Campbell and Elliott[3a] did not mention finding block in forty-two electrocardiograms taken in a series of one hundred patients with paroxysmal supraventricular tachycardia. A few isolated cases of paroxysmal atrial tachycardia with block have been reported, but no large series has been studied.

Paroxysmal tachycardia does occur frequently in the youthful undamaged heart and is quite generally considered innocuous, but we cannot accept its presence as a guarantee that the heart is normal. We have furthermore found that block occurs much more frequently in patients with serious heart disease. The defective conduction complications may be of serious prognostic significance. The possible precipitating factors of serious paroxysmal tachycardias with A-V block have interested us.

HISTORICAL REVIEW

Sir Thomas Lewis[1] recorded with a polygraph, as early as 1909, A-V block in the presence of paroxysmal atrial tachycardia. At that time he described extensive observations in two cases, in the second of which there were frequent dropped ventricular beats which, at times, led to halving of the ventricular rate. The polygram (Fig. 14, p. 64) shows the conduction defect.

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Drury,[2] in 1924, reported an instance of paroxysmal tachycardia of nodal origin with variable retrograde A-V block. The published tracing shows gradual prolongation of the R-P interval, with eventual disappearance of the P wave, a "retrograde Wenckebach" phenomenon. In some portions of the tracing, where there is a long R-P interval, a reciprocal ventricular beat is recorded.

Sprague and White,[3] in 1925, found three cases of A-V block among fifty-six cases of paroxysmal tachycardia in which records had been taken at the Massachusetts General Hospital during the preceding decade; a total of 5,085 patients had electrocardiograms taken. The first case was that of a 48-year-old woman who had bilateral cervical ribs and was thought to have rheumatic mitral disease. The tracings indicated the presence of two ectopic auricular foci, one or the other being responsible for the numerous paroxysms. Although the ventricle was able to preserve 1:1 conduction with an auricular rate as high as 270 per minute, albeit with intermittent QRS aberration, on other occasions there was varying A-V block, 3:2, 2:1, 3:1, etc., at atrial rates as low as 200 per minute, with no definite relation between the rate and block. Digitalization was of benefit, and removal of the cervical ribs appeared to give partial relief. The patient was sensitive to quinidine.

The second case was that of a 23-year-old woman without definite heart disease. At an atrial rate of 220, the ventricular rate was 110; after exercise the grade of block decreased to 4:3 or 3:2, and was of the Wenckebach type. Digitalis was thought to be beneficial in decreasing the number of attacks. The third case recorded by Sprague and White was that of a 26-year-old man without physical abnormality. The electrocardiograms showed frequent atrial premature beats. Other tracings during paroxysms showed occasional prolongation of the P-R interval, but with conduction to the ventricle. On other occasions there was gradual prolongation of the P-R interval, with block varying from approximately 10:9 to 2:1.

Since Sprague and White's paper, isolated cases have been reported. William Dock[4] described an instance of paroxysmal atrial tachycardia with an atrial rate of 180 to 186, in which block varying from 2:1 to 4:1 was noted. He specifically differentiated this from atrial flutter because of the absence of evidence in any lead of continuous atrial electrical activity. Vagus and ocular pressure failed to affect the atrial rate, and did not raise the grade of A-V block above 4:1. Heyl[5] studied a white man, 50 years old, with early congestive heart failure, whose paroxysms appeared after digitalization. That the drug precipitated the paroxysms was clearly proved by alternating periods with and without digitalis; 2:1 block was found frequently. On one occasion, change from the supine to the sitting position was shown to convert 2:1 A-V conduction to 1:1. These changes also occurred spontaneously. Reflex vagal stimulation, ineffective without digitalization, after varying doses of digitalis

produced conduction effects ranging from 2:1, 3:1, and 5:1 block to complete ventricular standstill.

Laubry and Deglaude[6] reported an instance of supraventricular tachycardia with a rate of 200 per minute in which there was slight cyclic variation of the P-R intervals, and also alternation of the R waves. Brown[7] showed several instances of A-V block in paroxysmal tachycardia in his study of atrial mechanism disorders by means of an esophageal electrode. Geraudel[8] followed an interesting case from 1926 to 1931. When first seen, the patient, 63 years of age, with hypertension, had evidence of cardiac failure while the ventricular rate was 172 per minute. Sudden cessation of the symptoms was associated with a fall in the ventricular rate to 86, which was shown electrocardiographically to be due to 2:1 A-V block. Change in position might initiate a change in conduction; thus, lowering of the head, standing up, or change from side to side in bed would abolish the block. Later tracings showed Wenckebach periods, with 5:4 or 4:3 conduction. In 1928 auricular fibrillation developed and persisted until 1931, when he was last seen.

Maddox[9] studied carefully a patient with a persistently rapid atrial rate. While the rate was 160 per minute, carotid sinus pressure caused a 3:2 block of the Wenckebach type. Digoxin (0.5 mg.) was given intravenously, and slowed the atrial rate to 120, but with progressive prolongation of the P-R interval and dropped beats. On another day, when the patient was lying down, there was a ventricular rate of 56, with a 3:1 block. Exercise then caused a sudden rise of the pulse rate to 168; at this time, carotid sinus pressure led to an irregular pulse, with coupling. During sleep the ventricular rate fell to 80-90 as a result of A-V block, but, when the patient was awake, the heart rate rose to approximately 160. After thirty-six days in bed, the atrial rate had fallen to 70, but the abnormalities of the P wave persisted. Quinine, quinidine, acetylcholine, adrenalin, and atropine were used, but failed to abolish the abnormal mechanism. Three months later, the patient was seen again with a ventricular rate of 168 per minute, which slowed with pressure on the right carotid sinus. Pressure on the left side was without effect.

Fine and Miller[10] have recently reported their observations on a patient who precipitated paroxysms of tachycardia whenever he sat up or stood up, unless this tendency was controlled by quinidine or digitalis. The rate varied from 120 to 200 per minute, depending on the posture. One tracing showed Wenckebach periods, and another, electrical alternation of the QRS complexes. The authors attributed the postural influence to vagal inhibition, mediated either through reflexes from the lower extremities or the carotid sinus, or because of changes in the cerebral blood flow. In support of this concept that vagus inhibition may coincide with the onset of paroxysmal tachycardia, instances were cited

in which paroxysms were precipitated by atropine, by adrenalin, or by actual vagus nerve disease and degeneration.

In a study of the influence of carotid sinus hypersensitivity in cardiac arrhythmias, Tanney and Lilienfeld[11] described the case of a 9-year-old girl who had had chorea three months previously, without demonstrable cardiac damage. When seen by them she had acute rheumatic fever, with mitral and aortic valvulitis. During an attack of paroxysmal tachycardia in which the rate was 150 per minute, carotid sinus pressure was applied. This produced complete A-V block, with ventricular asystole for 8.4 seconds, while the atrial rate slowed to 60 to 84 per minute. Partial A-V conduction then was resumed with an atrial rate of 94, and increasing, but with 2:1 block for 5.4 seconds. This was followed by 1:1 conduction, but with prolongation of the A-V conduction time.

Two of the current texts on electrocardiography illustrate A-V block in supraventricular paroxysmal tachycardia. Scherf and Boyd[12] show 2:1 block and Wenckebach periods. Katz[13] illustrates delayed A-V conduction, with Wenckebach phenomena and electrical alternation, 2:1 block, and alternation of P-R conduction time and P-P cycle length. Few clinical data accompany these records.

Medical literature contains a few tracings which appear to justify a diagnosis of paroxysmal atrial tachycardia with A-V block, but which have been otherwise interpreted. For example, Marvin,[14] in his discussion of ventricular tachycardia with alternating complexes, includes a case (No. 3) which appears capable of being interpreted as follows: Fig. 9 shows an atrial rate of about 200, and the first part of the tracings shows Wenckebach periods, with 3:2 and 2:1 A-V block. When 1:1 conduction is present, there is QRS aberration, usually with alternation and delay in intraventricular conduction. Likewise, Katz' book contains figures whose interpretation might be open to question (Fig. 308c, 317d). Doumer[15] reported a case as nodal tachycardia which appears actually to be auricular flutter. The case reported by Savy, et al.,[16] shows variable prolongation in A-V conduction, with interference dissociation.*

THE CRITERIA FOR THE DIAGNOSIS OF PAROXYSMAL ATRIAL TACHYCARDIA

These difficulties in interpretation raise the question of the criteria which must be applied to substantiate the diagnosis of *auricular or atrial tachycardia,* and particularly its differentiation from flutter. The classical criteria set down by Lewis[17] need some modification. His definitions may be summarized as follows:

*In the few months since submitting this manuscript for publication, an excellent paper on this topic has appeared (Barker, P. S., Wilson, F. N., Johnston, F. D., and Wishart, S. W.: Auricular Paroxysmal Tachycardia With Auriculoventricular Block, AM. HEART J. 25: 765, 1943). During this time, also, nine additional cases of paroxysmal tachycardia with A-V block have occurred, bringing the total in our files to forty-nine cases.

Paroxysmal tachycardia is characterized by the following: (1) onset and ending are abrupt; (2) first atrial response is premature; (3) it ends with a pause; (4) atrial rhythm is remarkably regular, with a maximal difference of less than 0.01 second; (5) with rare exceptions, exercise, posture, atropine, and vagus stimulation do not affect the atrial rate; (6) duration of more than ten days is rare; (7) an anomalous P wave, indicating an ectopic focus, may be shown, although sometimes the difference from the P wave of sinus origin is very slight (this is particularly so in the cases showing A-V block); (8) QRS aberration is frequent.

Auricular flutter is characterized as follows: (1) It is usually an established condition, although occasionally it is transient and repeated; (2) the atrial rate varies from 220 to 370, averaging 300 per minute; (3) the atrial rate is constant; (4) the atrial rate is unaffected by exercise, posture, atropine, and vagal stimulation; (5) in Lead I the atrial complexes are diminutive; in Leads II and III they show a sharp ascent, a blunt summit, and a gradual return; (6) "the complexes are contiguous; the string is moving constantly and rests for no measurable period on a base line."

MODERN CRITERIA IN SUMMARY

There is sometimes great difficulty in differentiating paroxysmal atrial tachycardia, flutter, and sinus tachycardia. Although there are rules for general application, nearly all are subject to exceptions, as is well recognized, and we have no absolute criteria for the diagnosis of ectopic atrial tachycardia. A sudden onset and termination are more likely in paroxysmal tachycardia than in flutter; a long duration is more likely in flutter. Carotid sinus pressure is much more likely to affect A-V conduction in flutter than in tachycardia; high atrial rates (above 280) are almost invariably the result of flutter. Moderately high atrial and ventricular rates (about 200, rarely above 240 or 260, and only occasionally below 160) are found in paroxysmal atrial tachycardia. All of these are helpful, but not absolute, rules. When the atrial rate is below 180 or 160, clear demonstration of an aberrant, ectopic P wave distinguishes paroxysmal from sinus tachycardia. A definite isoelectric segment indicating suspension of auricular activity, and hence the absence of a circus mechanism, distinguishes tachycardia from flutter. No other absolute criteria are available. Employing these, however, we have found a goodly number of instances of A-V conduction disturbance during paroxysms of atrial tachycardia. We have had a few cases in which all three cardiac mechanism disorders, namely, atrial tachycardia, flutter, and fibrillation, have been recorded, so that we cannot argue that the presence of flutter at one time rules out the possibility of paroxysmal tachycardia at another time. Paroxysmal tachycardia may be the result of a different type of circus rhythm.

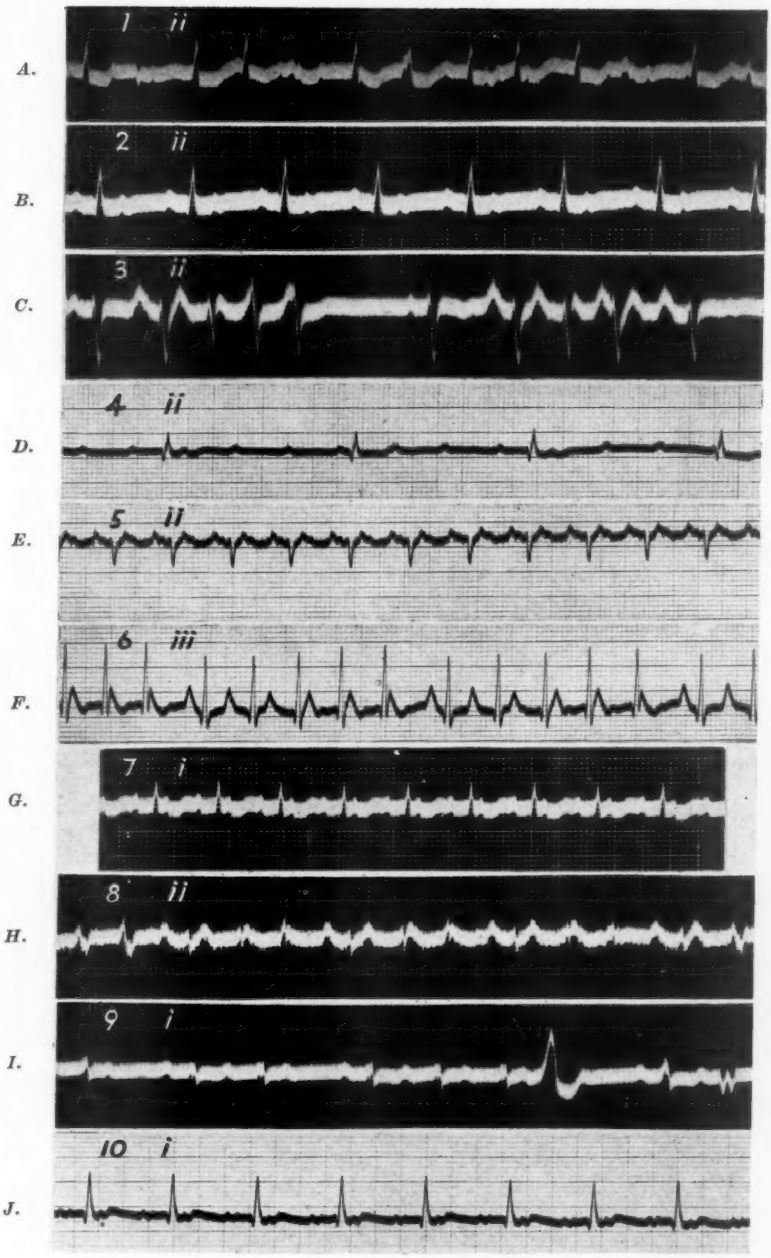

Fig. 1.

ABSTRACTS OF CASE RECORDS

CASE 1.—M. G., a colored man, aged 46 years, John Sealy Hospital No. 29976, was admitted Jan. 17, 1931, with congestive heart failure and general anasarca. The previous year he had hyperthyroidism and atrial fibrillation, and a thyroidectomy was done. The myocardial damage had persisted. During his first four days in the hospital he received 24 grains of digitalis, which caused a brisk diuresis and a rapid loss of 21 pounds in weight.

On the fifth hospital day his heart rate was 176 per minute, the rhythm was regular, and electrocardiograms showed that he had atrial paroxysmal tachycardia. Six cubic centimeters of digifolin were given intramuscularly, and twenty minutes later the rate had increased to 190 per minute and the electrocardiogram (Fig. 1, *A*, Lead II) showed a variable grade of A-V block of the Wenckebach type, usually 4:3 and 3:2. Note the slight differences in the cycle length.

The patient died on his sixth hospital day. At necropsy his heart was found to be enlarged, weighing 530 grams. There were myocardial scarring and fibrinous pericarditis. The lungs showed infarcts as well as some pneumonitis. The kidneys showed arteriolar disease. There were bilateral hydrothorax and chronic passive congestion.

CASE 2.—A. R., a colored man, aged 47 years, John Sealy Hospital No. 17146, was admitted Nov. 19, 1933, with congestive heart failure of about two months' duration. The failure had been precipitated by a respiratory infection. On November 25 hemoptysis was noted, and on that day 12 c.c., equivalent to 6 cat units, of digalen were given in the morning and 2 cat units in the afternoon. The following day, November 26, 4 more cat units were given, and electrocardiograms taken the same day (Fig. 1, *B*, Lead II) showed that he had atrial tachycardia with an atrial rate of 184 and a ventricular rate of 92, indicating 2:1 A-V block. Two days later there was sinus rhythm with a rate of 90 per minute. The patient's blood pressure was 98/74. The clinical diagnosis was arteriosclerotic heart disease, with cardiac enlargement and congestive heart failure. He improved under further treatment and was discharged from the hospital Dec. 24, 1933.

CASE 3.—W. H., a white man, aged 65 years, Electrocardiogram No. 1179, was seen as an outpatient on May 17, 1933, because of dull, aching pain in the precordial area and upper abdomen. His blood pressure was 180/80 and he showed signs of generalized arteriosclerosis. Previous electrocardiograms had shown numerous atrial premature beats. On May 17 electrocardiograms (Fig. 1, *C*, Lead II) showed short paroxysms of atrial tachycardia at a rate of 272 per minute, with a varying Wenckebach type of A-V block. No medication was given at this time, although quanidine was used later for control of these paroxysms.

CASE 4.—J. K., a colored man, aged 56 years, John Sealy Hospital No. 45983, was admitted Oct. 4, 1934, with congestive heart failure which had been present for four months. His blood pressure was 168/130; there was marked peripheral arteriosclerosis; gallop rhythm was present; and there was fluid in the right pleural sac, with extensive dependent edema. On October 3 electrocardiograms showed an atrial rate of 187, with 2:1 heart block. On October 4 the atrial rate was 194; on October 5 there was sinus rhythm with a rate of 90 per minute. On October 6 the atrial rate was 158, and carotid sinus pressure increased the grade of A-V block to 4:1 and higher (Fig. 1, *D*, Lead II). On October 8 the atrial rate had gone up again to 190 per minute. Later tracings showed sinus rhythm.

The patient had a stormy course in the hospital, with multiple emboli, including one in the left leg necessitating amputation, and another in the lower lobe of the right lung. The last embolus produced right-sided hemiplegia, shortly after which he died. Necropsy showed that the heart was enlarged, weighing 640 grams. There

was marked arteriosclerosis of the coronary vessels, with an old myocardial infarct and mural thrombosis at this point. Pulmonary infarction was present, and there were thrombi in the aorta and iliac arteries.

CASE 5.—L. B., a colored man, aged 83 years, John Sealy Hospital No. 46741, was admitted Feb. 12, 1935, with moderate congestive heart failure. He had had the anginal syndrome and congestive failure for two years. The blood pressure was 130/100. The heart was enlarged to the left and the aortic second sound was markedly accentuated. Previous electrocardiograms had shown marked left axis deviation and numerous ventricular and atrial premature contractions. On March 2 the electrocardiogram (Fig. 1, *E*, Lead II) showed an atrial rate of 250 per minute, with 2:1 A-V block. On March 8 the atrial rate was 255 per minute, and there was still a 2:1 A-V block; on this day 8 cat units of digalen were given in four doses, and this changed the mechanism to sinus rhythm at a rate of 100 per minute.

After this he improved markedly, and was discharged April 19. However, he returned to the hospital with congestive failure on May 23, and again on Sept. 6, 1935, at which time he died. At necropsy the heart weighed 560 grams and showed marked coronary arteriosclerosis and a thrombus in the right auricular appendage. The kidneys showed arteriolar disease.

CASE 6.—J. V., a white woman, aged 27 years, Electrocardiogram No. 787, had been under observation as an outpatient for fourteen years because of frequent paroxysms of tachycardia. She had no demonstrable heart disease. There were numerous electrocardiographic records of paroxysms on file, with an atrial rate of 146 to 174 per minute. In an attempt to control her paroxysms she had been started on moderate doses of digitalis on Nov. 1, 1934, and had been maintained on 1½ grains of digitalis folia every day thereafter. An electrocardiogram (Fig. 1, *F*, Lead III), taken on March 5, 1935, showed A-V block. The atrial rate varied from 164 to 187, and there was a slight degree of A-V block of the Wenckebach type, varying from 6:5 to 23:22, and less. The curves after digitalization were the only ones over a long period that showed any block; all curves taken during subsequent attacks have shown 1:1 A-V conduction.

CASE 7.—C. B., a white man, aged 50 years, John Sealy Hospital No. 48378, was admitted June 20, 1935, with the symptoms and signs of congestive heart failure of a year's duration. The blood pressure was 110/70; pulsus alternans was present. Numerous electrocardiograms, taken from June 27 to July 2, showed atrial tachycardia; the atrial rate varied from 150 to 186. In all the tracings there is 2:1 A-V block (see Fig. 1, *G*, Lead I). Note that the cycle which contains the QRS complex is shorter. Digitalization was begun on the day after admission and maintained during his hospital stay, without effect on the cardiac mechanism.

He continued to lose ground, and died on July 5, 1935. Necropsy showed coronary arteriosclerosis. The heart weighed 450 grams. He also had hemorrhagic pericarditis, pleuritis, syphilitic leptomeningitis, and hypostatic pneumonia.

CASE 8.—H. P., a white man, aged 53 years, John Sealy Hospital No. 51712, was admitted June 3, 1936, with congestive heart failure which had been present for three months. Anginal pain had been present for three weeks. Electrocardiograms (Fig. 1, *H*, Lead II) taken before admission, on May 19, 1936, had shown atrial tachycardia, a rate of 200 to 203, and 4:3 and 3:2 block. The next day the atrial rate was 150, with 1:1 conduction. On June 7, 10½ grains of digitalis were given and produced vomiting. The following day mercupurin was given, and, the day after this, atrial tachycardia was present with an atrial rate of 182 per minute, but without A-V block. The next day, June 10, he had sinus rhythm at a rate of 128 per minute. The patient died June 14, his eleventh hospital day. Necropsy showed syphilitic aortitis. The heart weighed 480 grams. There was a thrombus in the right auricular appendage, and multiple pulmonary infarcts were found.

CASE 9.—J. G., a colored man, aged 60 years, John Sealy Hospital No. 44449, was admitted June 29, 1936, with congestive heart failure. He had been in the hospital several times in the preceding seven years with similar symptoms and signs, and hypertension as high as 200/130. The blood pressure at this time was 130/100. For several years he had been maintained on digitalis at intervals. Previous electrocardiograms had shown, among other abnormalities, prolonged A-V conduction time. Electrocardiograms (Fig. 1, *I*, Lead I), in the morning of July 1, showed an atrial rate of 143, with 8:7 and 3:2 A-V block and Wenckebach periods. In the afternoon the atrial rate was 120 per minute, without block. Subsequent tracings showed sinus rhythm. He gradually improved on digitalis and theocalcin and was discharged Aug. 28, 1936.

CASE 10.—F. M., a white man, aged 56 years, John Sealy Hospital No. 45030, was admitted Aug. 24, 1936, with congestive heart failure due to hypertension and arteriosclerotic heart disease. He had had the anginal syndrome since 1933, and three days after admission he developed pulmonary infarction associated with jaundice. On August 28 he was started on digitalis in a dose of 1½ grains three times a day, and this was continued until September 10, when the dosage was reduced to one tablet daily. On September 12, electrocardiograms (Fig. 1, *J*, Lead I) revealed atrial tachycardia with an atrial rate of 179 per minute and 2:1 A-V block. Note the shortening of the cycle containing the ventricular beat. On September 11 he suffered myocardial infarction, which caused his death on September 14. At necropsy his heart weighed 580 grams; infarction of the myocardium was present, with mural thrombosis associated with multiple infarcts of the lungs, spleen, and brain.

CASE 11.—C. D., a colored man, aged 36 years, John Sealy Hospital No. 52195, was admitted Nov. 20, 1930, with congestive heart failure that had been present for five months. The blood pressure was 160/120, and the physical signs were those of myocardial failure. On December 13 he was given 19½ grains of digitalis by mouth, and the next day electrocardiograms showed paroxysmal atrial tachycardia; the rate was 169 per minute, with 1:1 A-V conduction. On December 15, 23 grains of quinidine were given, and an electrocardiogram (Fig. 2, *A*, Lead II), on December 16, showed that the tachycardia continued, with the atrial rate varying from 190 to 218, but now with 5:4 and 3:2 Wenckebach A-V block. Note that when the block is present, the cycle that contains the ventricular beat is much shorter. The following day there was sinus tachycardia with a rate of 136 per minute. The patient died Jan 6, 1937, and necropsy was not obtained.

CASE 12.—F. M., a white man, aged 48 years, John Sealy Hospital No. 37597, was admitted Feb. 5, 1938. Congestive heart failure had been present for one month before admission. The previous year the patient had had a gastrointestinal hemorrhage, and anemia persisted. The blood pressure was 218/134, and uremia was also present. Digitalis had been given for one week before admission to the hospital, and was continued at a rate of 1½ grains daily. Electrocardiograms (Fig. 2, *B*, Lead II), on the day of admission, showed an atrial rate of 200 per minute, with 4:3, 5:4 Wenckebach block. Note the progressive aberration of QRS complexes. After 9 grains of quinidine on February 6, and again on February 7, sinus tachycardia was recorded at a rate of 105 per minute. Nitrogen retention was progressive; papilledema developed, and the patient died of uremia on March 20, 1938.

CASE 13.—J. R., a colored woman, aged 53 years, John Sealy Hospital No. 57901, was admitted Feb. 24, 1938, with congestive heart failure which had been present for one month. She complained also of diarrhea, greenish vision, and vomiting. Before admission she had been given tincture of digitalis in a dose of 60 drops daily for nine days. To this medication had been added powdered digitalis leaf in a dose of 1½ grains three times daily. No digitalis was administered in the hospital

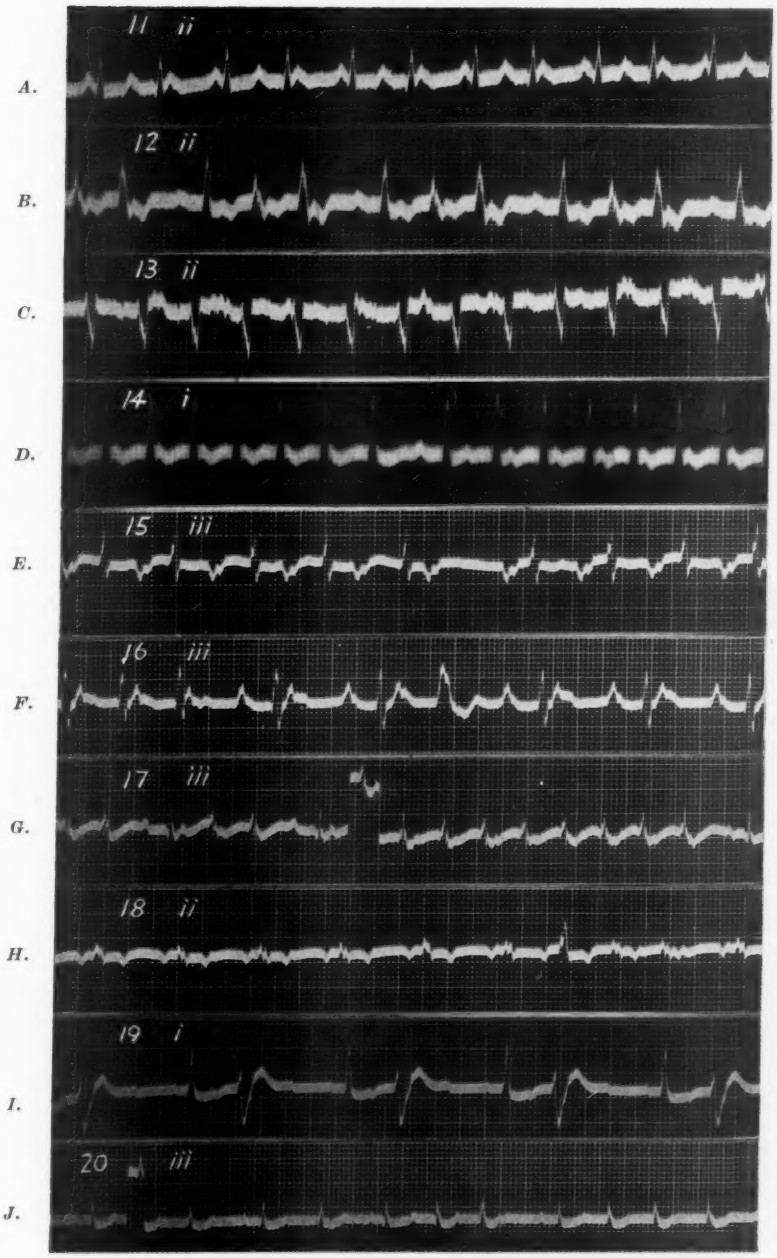
11 ii
A.
12 ii
B.
13 ii
C.
14 i
D.
15 iii
E.
16 iii
F.
17 iii
G.
18 ii
H.
19 i
I.
20 iii
J.

Fig. 2.

because of the obvious previous overdosage. Electrocardiograms (Fig. 2, *C*, Lead II), taken on admission, showed paroxysmal tachycardia of nodal origin, with a rate of 165 per minute. P waves could be made out, showing an independent atrial tachycardia of 125 per minute, with complete A-V dissociation. By March 1, the rhythm was sinus tachycardia, with delayed A-V conduction.

CASE 14.—K. L., a white man, aged 45 years, John Sealy Hospital No. 57248, was admitted March 7, 1939, with congestive heart failure. The blood pressure was 252/168. A lumbar sympathectomy had been performed fourteen months previously because of this marked hypertension, but very little benefit had resulted. In the five days before admission, the patient had taken 15 1½-grain tablets of digitalis. On March 13, 2.5 mg. of digoxin were given intravenously, and on March 14, it was found that atrial fibrillation had developed. On March 17, 18, and 19, 1½-grain doses of digitalis were given twice daily. Electrocardiograms (Fig. 2, *D*, Lead I), on March 20, showed paroxysmal atrial tachycardia, with an atrial rate of 182 per minute; 8:7 and 7:6 A-V block was present. On March 22, digitalis was begun again; paroxysmal tachycardia recurred with an atrial rate of 193, with rare dropped ventricular beats. During this time, nitrogen retention had progressively increased, and the patient died, on March 29, of uremia. At necropsy the heart weighed 670 grams and there was marked nephrosclerosis. A few atheromatous plaques were noted in the aorta.

CASE 15.—A D., a white girl, aged 14 years, John Sealy Hospital No. 66298, was admitted April 17, 1940. For four years she had been bothered by attacks of dyspnea which was associated with tachycardia, vertigo, and pain in the chest. The blood pressure was 78/56, and the heart rate was 188 per minute. Electrocardiograms showed that the atrial rate, on April 17, was 158 to 188; on April 18, 187 to 190; on April 19, 130; and on April 22, 120. Quinidine in a dose of 5 grains was given four times daily on April 19 and April 21. On April 19, carotid sinus pressure caused one dropped beat. On April 24 and 25, 1½ grains of digitalis were given three times daily. On April 26 and 27, digitalis was given twice daily and once daily thereafter. In electrocardiograms (Fig. 2, *E*, Lead III), taken April 26, the atrial rate was 125, with occasional dropped beats and Wenckebach periods. On April 30 the rate was 115, and there were frequent blocked beats. The atrial rate showed marked variation. The treatment caused a slowing in the atrial rate, although the ectopic pacemaker persisted during the whole period. On May 16 the patient had a sudden attack of extreme tachycardia, with a rate of 250 per minute; this was probably also ectopic, as the others had been for four years. No measures resulted in improvement. Necropsy showed a heart which weighed 430 grams and was markedly dilated and hypertrophied. There was a patent ductus arteriosus which measured 1 mm. in diameter. The aorta was very small, measuring only 50 mm. in circumference at the ring. Congenital hypoplasia of the aorta was considered to be the primary cardiac disease.

CASE 16.—D. E., a colored man, aged 45 years, John Sealy Hospital No. 67100, was admitted Sept. 17, 1940. This patient had been in the hospital twice previously in 1940, with congestive heart failure due to hypertensive heart disease. The blood pressure was 180/110. Pulsus alternans and gallop rhythm were present, and mild congestive failure was evident. The patient had been maintained on 1½ grains of digitalis leaf daily since his first hospital admission on June 7, 1940; on July 3 bigeminy had been noted, probably due to digitalis overdosage. When first seen on September 17, electrocardiograms showed an atrial rate of 152 per minute with 1:1 A-V conduction. Deep respiration slowed the atrial rate from 150 to 144 and there was A-V block varying between 2:1 and 5:4. Carotid sinus pressure produced 2:1 to 6:5 block, with frequent ventricular escapes, as shown in the electrocardiograms (Fig. 2, *F*, Lead III). Quinidine was administered, and the atrial rate

slowed from 158 to 143, with variable block, sometimes as high as 3:1, with ventricular escape. Cycles containing ventricular beats measured 0.40 second and blocked cycles measured 0.45 second. Deep respiration and carotid sinus pressure produced A-V block, the grade of which was increased after quinidine administration. A few hours after the use of quinidine, the paroxysmal tachycardia disappeared.

CASE 17.—R. Z., a white woman, aged 63 years, John Sealy Hospital No. 67926, was admitted Aug. 15, 1940, in a semicomatose condition. She had been weak for about four days, and her relatives stated that she had had dyspnea and edema, nocturnal coughing, orthopnea, and hypertension, for two years. The blood pressure was 190/80, and she had Cheyne-Stokes respiration, but there was no evidence of congestive heart failure. On August 28 an attack of paroxysmal tachycardia, with an atrial rate of 162, was recorded. It stopped spontaneously. On September 4 another attack was recorded, with an atrial rate varying from 188 to 250, and with aberrant QRS complexes. This attack was stopped by 3 grains of quinidine every hour for ten doses. On other occasions there were frequent atrial premature beats. On November 6 she had another paroxysm, and electrocardiograms (Fig. 2, *G*, Lead III) showed an atrial rate of 160 to 169, with a Wenckebach period type of A-V block varying from 4:3 to 11:10, and less. Death occurred Nov. 17, 1940. The final diagnosis was generalized arteriosclerosis, with particular involvement of the coronary and intracranial arteries.

CASE 18.—T. R., a white man, aged 49 years, John Sealy Hospital No. 66787, was admitted Oct. 15, 1940. Congestive heart failure was present and had been present on previous occasions. The blood pressure was 128/100, gallop rhythm was present, and pulmonary congestion was marked. Digitalis (1½-grain tablets) was given three times a day for four days, from November 22 to November 25, then one tablet daily until November 27. Beginning November 28, three 1½ grain doses were again given daily, until December 8. On December 1, 2 c.c. of mercupurin were injected intravenously and resulted in considerable diuresis; on December 2 atrial fibrillation developed. Eighteen grains of quinidine were given that day and stopped the fibrillation. The following day, December 3, electrocardiograms (Fig. 2, *H*, Lead II) showed atrial tachycardia with an atrial rate varying from 150 to 188 per minute, and block, varying from 2:1 to 9:8, of the Wenckebach type. Note here also the variation of the cycle length. The patient died December 14, and necropsy showed a heart weighing 600 grams, with slight coronary arteriosclerosis. There were thrombi in both ventricles and in the right atrium, and there were multiple pulmonary infarcts. Nephrosclerosis was present, and there was, of course, chronic congestion in the viscera.

CASE 19.—V. N., a colored woman, aged 38 years, John Sealy Hospital No. 70439, was admitted April 9, 1941. She showed marked congestive heart failure which had been present for about two months. At home she had taken some small brown pills of uncertain nature. The blood pressure was 200/20 and the other physical signs were those of syphilitic aortic regurgitation. Electrocardiograms, on admission, showed sinus tachycardia, left axis deviation, depression of the S-T segments in Leads I and II, and negative T waves in Leads I and IV F. Digoxin (1 mg.) was given intravenously, and fifteen minutes later she vomited and had bigeminy and trigeminy. Electrocardiograms (Fig. 2, *I*, Lead I), taken at this time, showed an atrial rate of 190 per minute, with 4:1 A-V block and frequent ventricular escape, usually giving bigeminy. Death occurred a few hours later, and necropsy showed typical syphilitic aortitis and aortic regurgitation. The heart weighed 430 grams.

CASE 20.—J. W., a white man, aged 81 years, John Sealy Hospital No. 69078, was admitted March 17, 1941, because of prostatic disease. Prostatic resection was done March 26. On April 7 the patient had a short attack of paroxysmal dyspnea, which recurred on April 16. Electrocardiograms, the next day, showed short runs of paroxysmal atrial tachycardia. Digitalization was begun at this time, with 13½ grains of the powdered leaf of digitalis the first day, and maintenance doses of 1½ grains daily, afterwards. Electrocardiograms (Fig. 2, *J*, Lead III), on April 28, showed paroxysmal tachycardia with an atrial rate of 179 per minute; 6:5, 4:3, and 3:2 A-V block of the Wenckebach type was present. Quinidine, which was given on this day and on April 29, terminated the paroxysm. Electrocardiograms both before and after this attack showed frequent atrial premature beats.

CASE 21.—G. S., a colored woman, aged 24 years, John Sealy Hospital No. 71436, was admitted June 23, 1941. She had had paroxysms of tachycardia since childhood. At the time of her admission she was seven months pregnant, and had had frequent paroxysms in the preceding two months. The attack which brought her to the hospital had lasted for six days, and had been associated with difficulty in hearing, dyspnea, edema, and precordial pain radiating to the right shoulder. She had had three previous miscarriages. She had anemia, with a hemoglobin of 55 per cent. The blood pressure was 120/75. The heart was normal in size and no cardiac lesion could be demonstrated. When first seen, the heart rate was 220 per minute, the beating regular, and the rhythm was not affected by carotid sinus pressure. Eight cubic centimeters of cedilanid, equivalent to 1.6 mg., was injected intravenously, and three minutes later there was a sudden slowing of the heart rate to 120 per minute. Tachycardia recurred thirty-six hours later, and at this time 8 c.c. more of cedilanid were injected. Immediately afterwards, electrocardiograms (Fig. 3, *A*, Lead I) showed an atrial rate of 118 per minute, with, roughly, 7:5 A-V block. The form of the P waves indicated that the ectopic focus was still effective. During the paroxysms of tachycardia, QRS aberration was present. At the termination of the paroxysm, gradual, stepwise return of intraventricular conduction to normal could be demonstrated. In later paroxysms, digitalis extract (Upjohn, 5 cat units in 10 c.c.), intravenously, stopped the attack immediately. Prostigmine was effective on one occasion, although at several other times it was not. Magnesium sulfate by vein was ineffective. The paroxysms were best controlled by the regular administration of quinidine, but even then occasional short paroxysms occurred.

CASE 22.—H. J., a white woman, aged 70 years, John Sealy Hospital No. 46412, was admitted July 4, 1941. She had had a left-sided hemiplegia in 1934, at which time her blood pressure was 190/140. Since then she had had several syncopal attacks, and for several months she had had moderate congestive heart failure. On admission, the venous pressure was 17 cm. of water, and there were evidences of fluid in both pleural sacs. The blood pressure at this time was 130/84. On July 5 and 6, a transudate was removed from the left pleura by thoracentesis. On both July 6 and 7, Cheyne-Stokes respiration was noticed, and 7½ grains of aminophylline were given by vein for relief. On July 6, digitalis folia (1½ grains three times a day) was begun. The next day, tachycardia was present and the recorded rates varied from 207 to 255; when the rate was 207 per minute, there was 1:1 A-V conduction (Lead I, Fig. 3, *B*); when the rate was 222 per minute, the A-V conduction was 3:2 block of the Wenckebach type. When the rate was as high as 255 per minute, A-V conduction was only 2:1. Intraventricular conduction was also defective. On July 8 there was shifting of the pacemaker, with defective intraventricular conduction. It should be noted that before the paroxysmal tachycardia there were frequent atrial premature beats. The atrial tachycardia ceased after the administration of 5 grains of quinidine every hour for four doses.

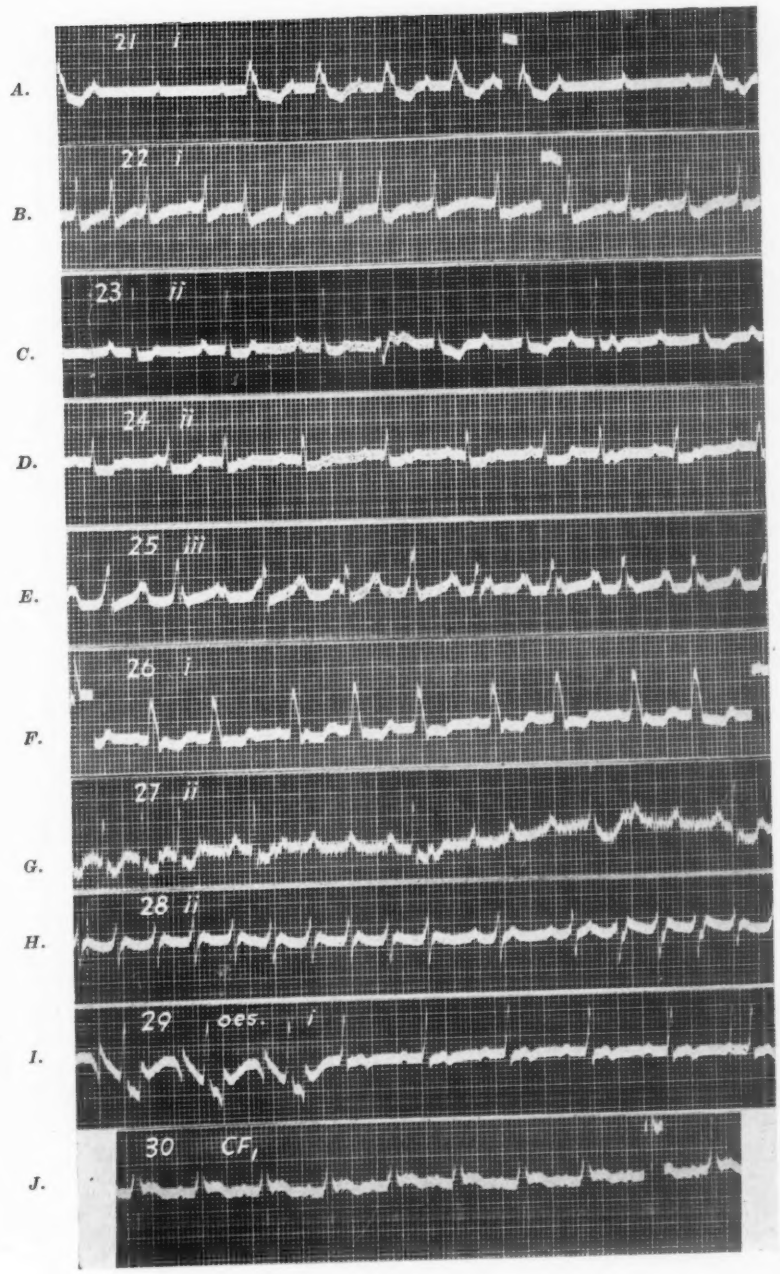
A.
21 i
B.
22 i
C.
23 ii
D.
24 ii
E.
25 iii
F.
26 i
G.
27 ii
H.
28 ii
I.
29 oes. i
J.
30 CF1

Fig. 3.

On the fifth hospital day the temperature rose, the dyspnea became more marked, and fluid reaccumulated in the pleural spaces; the patient became worse rapidly, and died on the seventh day. Necropsy showed that the heart weighed 365 grams. Purulent pericarditis, bronchopneumonia, peritonitis, and mild chronic passive congestion of all organs were found. There was an acute infectious process in the bladder and ureters, and encephalomalacia.

CASE 23.—W. W., a colored man, aged 38 years, John Sealy Outpatient Clinic No. 49248, was admitted Aug. 2, 1941. He had been seen in the Outpatient Department, three days before, with congestive heart failure which, according to his story, had been present four or five weeks. The blood pressure at this time was 160/130. There were cardiac enlargement, gallop rhythm, engorgement of the liver, and dependent edema. He had a history of a chancre in 1926. In the three-day interval he had taken sixteen tablets, of 1½ grain each, of digitalis leaf. Electrocardiograms, taken August 2, showed paroxysmal tachycardia with an atrial rate of 196 per minute and 1:1 A-V conduction. One milligram of prostigmine was given intramuscularly, and, after about ten minutes, there was transient slowing. Atrial tachycardia soon recurred; however, the auricular rate was only 182 per minute and there was 2:1 A-V block. Carotid sinus pressure had had no effect before, but at this time carotid sinus pressure and deep respiration increased the A-V conduction disturbance. Fig. 3, *C*, Lead II, shows A-V block of 2:1, and, in some parts, of 3:1. The atrial rate remained slow, and was from 156 to 176. During the period of block there were many nodal escapes and transient intraventricular conduction defects.

CASE 24.—P. J., a colored man, aged 76 years, John Sealy Hospital No. 78053, was admitted March 1, 1943, because of congestive heart failure. Dyspnea on exertion had been present for two years and gradually increasing edema had been noted for twelve months. For the preceding eighteen days these symptoms had been much worse. No medication had been administered.

The blood pressure was 200/90; the heart was conspicuously enlarged, and there were the usual evidences of chronic passive congestion of moderate grade. Atrial fibrillation was present and was shown in all electrocardiograms taken up to and including one on March 16.

Eighteen grains of powdered digitalis leaf were given by March 5, and after this date 1½ grains were given daily. Quinidine (3 grains three times a day) was given from March 12 to 20, at which time the dosage was increased to 5 grains three times a day. An electrocardiogram, taken March 20, showed atrial tachycardia, with an atrial rate of 166 to 171 per minute and 2:1 and 3:2 A-V block. The tracing taken March 22 showed an atrial rate of 214 per minute, with 2:1 A-V block. An hour later the auricular rate had dropped to 162, and there was 1:1 conduction. At this time 1 mg. of prostigmine was injected intramuscularly, and, with an atrial rate of 171 to 179, varying A-V block developed, either 2:1 or 3:2 of the Wenckebach type (Fig. 3, *D*, Lead II). The auricular rate was 176 on March 26, with 2:1 A-V block; after this date there was sinus rhythm with frequent auricular premature beats. Improvement was such that he was discharged April 4, 1943.

CASE 25.—W. L., a colored man, aged 74 years, John Sealy Hospital No. 73536, was admitted Nov. 18, 1941, because of genitourinary symptoms resulting from prostatic hypertrophy and a urethral stricture. His history further revealed nocturnal dyspnea. His blood pressure was found to be 200/140. Cheyne-Stokes respiration was present, as were the usual evidences of congestive heart failure. The Cheyne-Stokes respiration ceased after the administration of 7½ grains of aminophylline intramuscularly. Aminophylline was continued by mouth in a dose of 3 grains four times a day. On December 10, digitalis folia was begun in doses of 1½ grains three times a day, but only five doses were given. On December 12 it was found that the heartbeat was irregular, with an apical rate of 118 per minute. Electro-

cardiograms showed atrial tachycardia with an atrial rate varying from 167 to 196 per minute. At the lower rate there was 1:1 conduction, or, at most, 12:11 A-V block. At the higher rate there was 2:1 A-V block. On December 12, 25 grains of quinidine were given, and, on December 13, electrocardiograms (Lead III, Fig. 3, *E*) showed an auricular rate of 182 per minute with A-V block varying from 4:3 and 3:2 to 2:1. The patient died December 14 and necropsy showed that the heart weighed 590 grams. There were moderate coronary arteriosclerosis, marked nephrosclerosis, pneumonia, and generalized chronic passive congestion.

CASE 26.—E. W., a white woman, aged 65 years, John Sealy Hospital No. 74287, entered Jan. 5, 1942, because of paroxysmal nocturnal dyspnea and substernal pain. The blood pressure was 180/120 and the clinical signs were those of left ventricular failure. The electrocardiogram (Lead I, Fig. 3, *F*), taken on admission, showed an atrial rate of 260, with A-V block alternating between 2:1 and 3:1. Bundle branch block was also present. The tachycardia disappeared spontaneously, and later electrocardiograms showed frequent atrial premature beats. The bundle branch block persisted. Subsequent use of digitalis and coramine was followed by improvement.

CASE 27.—F. G., a colored man, aged 59 years, John Sealy Hospital No. 10629, was admitted Jan. 20, 1942. He had hypertensive and arteriosclerotic heart disease and had had dyspnea for six years. Substernal pain had been present for eight months and had been noted to increase during paroxysmal tachycardia. Electrocardiograms taken a year previously had shown atrial fibrillation, and the more recent ones showed reversion to sinus tachycardia. The blood pressure on admission was 136/96, and the physical signs were those of mild congestive heart failure. For three months the patient had been taking 3 grains of digitalis leaf daily. On the day of admission the electrocardiogram showed paroxysmal atrial tachycardia with an auricular rate of 214 per minute and 1:1 A-V conduction. The next day, January 21, electrocardiograms revealed an auricular rate of 200, with 2:1 A-V block. Carotid sinus pressure produced 3:1 and 4:1 A-V block, with occasional ventricular escape (Fig. 3, *G*, Lead II). Sitting up doubled the heart rate, and reclining caused it to drop back. Electrocardiograms taken nine months later showed that auricular fibrillation had appeared again.

CASE 28.—A. H., a colored woman, aged 46 years, John Sealy Hospital No. 19506, was admitted Jan. 15, 1942. Her blood pressure was known to have been elevated since 1926. She had been under treatment with digitalis for congestive heart failure, for four months before admission. Edema had beeen present for three weeks, but she had been taking digitalis only as she thought she needed it. When seen on this admission, the blood pressure was 250/160. The heart was markedly enlarged and there was massive edema. The blood nonprotein nitrogen level was elevated; the serum albumin was 3.44 per cent, and the globulin was 6.2 per cent. She had a rectal stricture caused by lymphogranuloma inguinale.

The day of admission, January 15, electrocardiograms showed auricular fibrillation. The next day, 1½ grain digitalis pills were administered three times a day, and this was continued during her hospital stay. On January 18 electrocardiograms showed paroxysmal tachycardia with an atrial rate of 194 per minute and 2:1 and 3:2 block. On January 20 sinus rhythm was present, with a rate of 133 per minute. On January 25 electrocardiograms (Lead II, Fig. 3, *H*) showed tachycardia with the auricular rate varying from 184 to 197 and a variable degree of A-V block—as little as 13:12 and as high as 2:1. There was also aberration of the QRS complexes, and the cycles containing the ventricular beats were shorter than those that were blocked. She died of uremia January 26.

At necropsy the heart weighed 515 grams and showed pericarditis. There were nephrosclerosis, bronchopneumonia, cerebral thrombosis, several pulmonary infarcts,

and chronic passive congestion. Lymphogranuloma inguinale, with rectal stricture, was found.

CASE 29.—A J., a colored man, aged 42 years, John Sealy Hospital No. 74824, was admitted Feb. 17, 1942, with congestive heart failure. He had hypertensive heart disease, with a blood pressure of 188/108. In addition to this he had renal insufficiency. The blood nonprotein nitrogen rose to 185 mg. per cent on March 12, a week before his death. It was learned that he had taken digitalis during January, but the exact amount was not known. Beginning February 18, the day after admission, he was given a 1½-grain digitalis tablet three times a day until February 23; the next day 1½ grains daily were given, and this dose was continued until his death. Electrocardiograms, on February 17 and 19, showed sinus tachycardia. On February 21, electrocardiograms (Fig. 3, *I*, Lead I, preceded by a short strip of an esophageal lead) showed an auricular rate of 179 to 190, with 2:1 A-V block. By February 24, the sinus tachycardia returned; on February 28, there was nodal rhythm, with a rate of 86 and shifting of the pacemaker. In the electrocardiograms (Fig. 3, *I*) the cycles containing the ventricular beats were 0.32 second, and those without a ventricular beat were 0.335 second. This patient died on March 20 of uremia. At necropsy the weight of the heart was 570 grams, and fibrinous pericarditis, benign nephrosclerosis, and an infarct of the right lung were found. The coronary arteries were not grossly involved.

CASE 30.—C. O., a white man, aged 73 years, John Sealy Hospital No. 44749, was admitted April 17, 1942, semicomatose, with Cheyne-Stokes breathing and a right-sided hemiplegia. The blood pressure was 180/104. The heart was enlarged and there was generalized arteriosclerosis. The signs of congestive failure were not conspicuous; the venous pressure was only 13 cm. of water. On both April 17 and 18 he received 1 mg. of digoxin intravenously, and on April 19 and 20 he received 0.5 mg. In addition, 0.5 Gm. of aminophylline was given by vein on April 18, 19, and 20. On April 18, the record showed atrial tachycardia with an atrial rate of 240 per minute and 2:1 block. Electrocardiograms on April 21 (Fig. 3, *J*, Lead CF_1) showed an atrial rate of 230 per minute, with 2:1 block. On April 24, sinus rhythm, with a rate of 75 per minute, was recorded. On May 2 electrocardiograms showed atrial flutter, which was controlled by quinidine on May 3 and 4. On May 4 sinus rhythm was recorded; but on May 5 atrial fibrillation was present.

CASE 31.—J. H., a white man, aged 79 years, John Sealy Hospital No. 61445, was admitted June 9, 1941, in a prolonged, persistent attack of tachycardia, with evidences of heart failure. He had been known to have paroxysms over a period of six years. Carotid sinus pressure had usually been without effect, and he had been taking 5 grains of quinidine three times a day. He had benign prostatic hypertrophy, and required frequent catheterization. Eighteen months before he had had a transurethral resection. Most of his preceding attacks had lasted not over two hours. The attack of June 9 had lasted more than twenty-four hours, and had produced dyspnea, pulsus alternans, pulmonary and hepatic congestion, and edema of the lower extremities. The neck veins were distended and there was Cheyne-Stokes breathing. The blood pressure was 128/88. The previous electrocardiograms, over a period of years, showed right bundle branch block with many paroxysms of tachycardia. On June 9, at 11:30 P.M., shortly after admission, he was given 1.2 mg. of cedilanid intramuscularly, and the next morning, at 9 o'clock, he was given 0.4 mg. more. This dose of 0.4 mg. was repeated that evening and again the next day. An electrocardiogram (Lead II, Fig. 4, *A* upper), with carotid sinus pressure, on June 10, showed atrial tachycardia with an average rate of 162 per minute and varying degrees of A-V block, 6:5 and more, to 6:1, with ventricular escape. On June 13, with the atrial rate at 165, and 1:1 conduction (Fig. 4, *A* lower, Lead I), there was alternation of cycle length (between 0.315 second and 0.37 second).

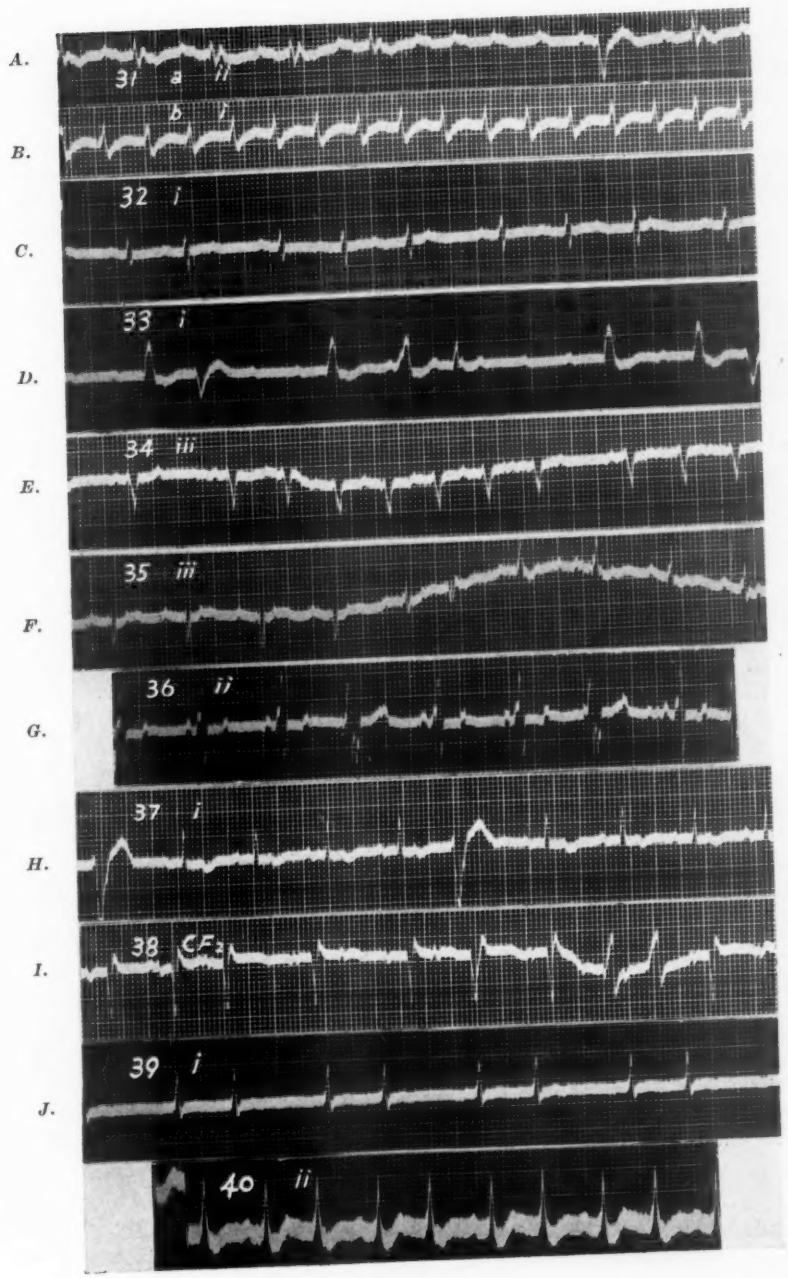
A.
31 a ii
B.
b i
32 i
C.
33 i
D.
34 iii
E.
35 iii
F.
36 ii
G.
37 i
H.
38 CF2
I.
39 i
J.
40 ii

Fig. 4.

Other drugs used were coramine and aminophylline, both by mouth. Death occurred March 31, 1943, as a result of gangrenous cystitis.

CASE 32.—O. H., a white woman, aged 25 years, John Sealy Hospital No. 76594, was admitted July 2, 1942. This patient had had a fever for four months, edema of her eyes, feet, and legs, and abdominal distention. She was found to have subacute bacterial endocarditis, and it was thought that she also had chronic glomerulonephritis. In addition, there was evidence of congestive heart failure. On July 5, 6, 7, and 8, she was given four tablets of digitalis of 1½ grains each. On July 9 she received two tablets, and, after that, one tablet daily. Sinus rhythm had been present on July 3. On July 9, electrocardiograms (Lead I, Fig. 4, *B*) showed a short paroxysm of atrial tachycardia; the atrial rate was 150 to 160, with 2:1 and 3:1 A-V block. Subsequent electrocardiograms showed sinus rhythm, with occasional premature atrial beats. In one tracing there was a short paroxysm of auricular fibrillation.

CASE 33.—H. H., a white man, aged 64 years, John Sealy Hospital No. 75738, was admitted June 26, 1942, with congestive heart failure. He had been in the hospital during the preceding month because of congestive heart failure. The blood pressure was 163/124, and there were the usual symptoms and signs of myocardial insufficiency. On June 27, the day after admission, he was given 8 c.c. of digilanid by vein. Digitalization was maintained by the administration of 1½ grains of digitalis leaf twice daily. On July 15, he was given 2 c.c. of mercupurin, which resulted in a satisfactory diuresis. Electrocardiograms had shown prolonged A-V conduction. On July 17, he was found to have paroxysmal atrial tachycardia with an atrial rate of 162. On July 18, the electrocardiogram (Lead I, Fig. 4, *C*) showed a rate of 156 per minute, with 2:1 block, occasional periods of 4:1 block, and ventricular escape. Bundle branch block was also present. Later electrocardiograms showed again the prolonged P-R interval of 0.24 second. The patient died on July 22. At necropsy the heart weighed 450 grams. There were bilateral pulmonary infarcts, both old and recent. Pleural effusion and bronchopneumonia were present. Myocardial hypertrophy, with fibrosis of the myocardium, was demonstrated microscopically. There were generalized arteriosclerosis, nephrosclerosis, and chronic passive congestion of the viscera.

CASE 34.—M. G., a white man, aged 46 years, John Sealy Hospital No. 77524, was admitted Aug. 27, 1942, because of arteriosclerotic heart disease which had led to symptoms of congestive heart failure for four months. Two days after admission he was given 9 grains of digitalis folia, and the following day he was given 6 grains more. This latter dose was repeated on August 31 and September 1. Beginning September 2, a daily dose of 1½ grains was used. On August 28, the day after admission, the electrocardiograms showed sinus rhythm, with a rate of 79 per minute. By August 30, however, the electrocardiogram (Lead III, Fig. 4, *D*) showed atrial tachycardia with an auricular rate of 150 per minute and A-V block of 3:2, 6:5, and less. Atrial premature beats had been seen on previous tracings, and, on August 31, atrial fibrillation developed. This persisted until October 21, at which time sinus rhythm appeared.

CASE 35.—D. N., a white man, aged 53 years, John Sealy Hospital No. 37379, was admitted Sept. 8, 1942. He had been seen in 1932, when he was suffering from hypertensive encephalopathy; the blood pressure at that time was 190/110. At this admission he complained of severe substernal pain of three days' duration, associated with dyspnea for one day. Examination showed that the blood pressure was 220/120, and there were the usual signs of congestive heart failure. The patient had been given eleven tablets of digitalis folia, of 1½ grains each, during the four days preceding admission. The day of admission, September 8, he was given two injections of digilanid, 3 cat units each, six hours apart. The following day, an electrocardio-

gram was taken, and the chest leads showed evidence of anterior myocardial infarction. It also showed (Fig. 4, *E*, Lead III) an atrial rate of 193 to 207 per minute, and 2:1 A-V block. Occasionally, the A-V block was only 3:2, and of the Wenckebach type. There was aberration of the QRS complexes. The cycle which contained the ventricular beat was 0.29 second, and that which had a blocked auricular beat was 0.31 second. Digitalis was stopped and quinidine was administered. The following day sinus rhythm was re-established.

CASE 36.—J. M., a colored man, aged 51 years, John Sealy Hospital No. 16217, was admitted Oct. 21, 1942. This man had had congestive failure since 1940. He had hypertensive and arteriosclerotic heart disease, with a blood pressure of 220/110. He had been taking digitalis irregularly, usually one and two tablets on alternate days. On admission, he had bigeminy and presented the usual evidence of congestive heart failure. On October 25 he had severe epigastric pain, and serial electrocardiograms showed evidence of acute myocardial infarction. A pericardial friction rub was heard the next day. Since the patient was already overdigitalized, mercupurin was employed to control his edema, and, on October 26, 28, and 30, 2 c.c. of mercupurin were injected intravenously. On October 26, electrocardiograms (Lead II, Fig. 4, *F*) showed atrial tachycardia, with rates varying from 171 to 193, and A-V block ranging from 3:1 to 3:2 to 2:1, often with QRS aberration. The atrial cycles containing a ventricular beat measured 0.31 second. Those containing the blocked atrial beat measured 0.35 second. On October 27 electrocardiograms showed auricular tachycardia at the rate of 115 per minute, but with the pacemaker in the ectopic focus recorded on October 26. This was stopped by carotid sinus pressure. On October 30 the same ectopic focus produced a tachycardia at the rate of 150 per minute, with only occasional dropped ventricular beats. This patient responded poorly to treatment, gradually became worse over a period of two months, and died Jan. 1, 1943. The necropsy showed great cardiac hypertrophy and dilatation, with coronary arteriosclerosis. There were renal arteriolar changes and chronic passive congestion of the viscera.

CASE 37.—L. H., a white woman, aged 61 years, John Sealy Hospital No. 80555, was admitted March 19, 1943, with symptoms and signs of hypertensive heart disease. Congestive failure had appeared four years previously but had been controlled by the daily use of digitalis; however, the dosage was rather irregular, and had been occasionally as much as 5 grains daily. Two weeks before admission, there had been an exacerbation of her dyspnea. The blood pressure was found to be 280/180. The heart was enlarged to the anterior axillary line, and there were the usual manifestations of passive congestion.

Beginning March 20, 1943, 7½ grains of aminophylline were given daily, intramuscularly, and two 1½-grain tablets of digitalis were given March 20, 21, 22, and 23. On March 19, electrocardiograms showed sinus rhythm and a rate of 100 per minute. On March 22, she had auricular tachycardia, with an auricular rate of 207 to 214 and 2:1 A-V block (Fig. 4, *G*, Lead I). The next day she again had sinus tachycardia, with a rate of 103 per minute; only one short run of auricular ectopic beats appeared on the record.

CASE 38.—E. S., a colored woman, aged 65 years, John Sealy Hospital No. 75227, entered the hospital March 25, 1943, because of dyspnea and cough. She had been hospitalized twice in 1942 because of congestive heart failure due to hypertensive and arteriosclerotic heart disease. Numerous electrocardiograms, since March 22, 1942, had shown auricular premature beats, and, for a short period in August, 1942, auricular fibrillation had been present. Since Sept. 27, 1942, she had been attending the Outpatient Department intermittently, and had been maintained on 1½ grains of digitalis daily. Two weeks before admission, her own physician increased this dosage to 1½ grains three times a day. Palpitation and vomiting were noted three days before admission.

The blood pressure was 156/100. The heart was enlarged, as was the liver. The cardiac rhythm was irregular. Electrocardiograms, on March 26, 1943, showed many short runs of auricular premature beats. On March 29 and 31, the tracings showed auricular flutter. By April 1, the flutter had been replaced by sinus rhythm, with many auricular premature beats. April 5 the same mechanism persisted, with irregular A-V block (Fig. 4, *H*, Lead CF_2).

The flutter was terminated March 31 by quinidine (eight doses of 5 grains each). On April 1 only 5 grains of quinidine were used; but from April 2 to 5, 5 grains were given three times a day. On April 3 digitalis was begun in doses of 1½ grains daily.

CASE 39.—J. M., a colored man, aged 48 years, entered Charity Hospital Feb. 14, 1931, in an extreme stage of congestive heart failure. He had a cough and hemoptysis which suggested pulmonary infarction. Dizziness and tightness of the chest had been present for some time. He had been in the hospital a month previously with the same symptoms. He had a hard chancre in 1900. Conspicuous orthopnea and generalized anasarca were noted. He presented evidence of cardiac enlargement, and a striking gallop rhythm was heard. The blood pressure was 180/100. Râles were present at the bases of the lungs. There was some ascites. The edge of the liver could not be felt. The extremities were edematous. The urine was of low specific gravity (1.008), and the output was low. The blood nonprotein nitrogen was elevated to 60 mg. per cent. The blood serologic reactions were positive. On Feb. 14, 1931, he was given, intravenously, 5 c.c. of digalen at 5:45 P.M. February 15, he received 3 c.c. more of digalen intravenously. Electrocardiograms taken February 16 showed paroxysmal atrial tachycardia, with 3:2 block and a rate of 154 per minute (Fig. 4, *I*, Lead I). Tincture of digitalis in a dose of 30 minims was started February 21. The patient continued to grow worse and died March 4, 1931. No autopsy was done.

CASE 40.—M. C., a Negress, aged 22 years, entered Charity Hospital Jan. 26, 1928, with congestive failure and paralysis. Her symptoms began at the end of her pregnancy, three weeks before admission, when she had noticed attacks of severe weakness and dizziness. At the age of 20 years she had had severe malaria which lasted for several months. She had had mild attacks of tonsillitis, and occasionally aching in the shoulders, but no typical rheumatic fever. Her marital and family histories were negative. She was orthopneic, her tonsils were inflamed, her thyroid gland was enlarged, her heart was enlarged, and the rate was fast. There was gallop rhythm, and, at times, irregularities of rhythm were noted; her blood pressure was 121/62. The liver and abdomen were negative. The extremities were edematous and there was partial paralysis of the legs. The urine was of low specific gravity (1.005), and contained albumin and granular casts. Electrocardiograms taken on the day of admission showed paroxysmal tachycardia with an atrial rate of 206 to 222 and occasional dropped beats; the block at times was as much as 3:2 (Fig. 4, *J*, Lead II). According to the record, the patient had apparently received no medication, although she might have received digitalis before she left home. She died on the second hospital day, and no autopsy was done.

ANALYSIS OF ILLUSTRATIVE CLINICAL MATERIAL

Our clinical material has been derived from electrocardiograms taken on 8,800 patients over a period of about twelve years. Included are one hundred two examples of supraventricular paroxysmal tachycardia of varying duration. Study of these curves showed that there was failure of atrioventricular conduction in thirty-eight instances. Two additional cases from Charity Hospital in New Orleans are included. In others the A-V conduction time was relatively prolonged, but these cases were not

included because simple prolongation of the P-R interval in association with paroxysmal tachycardia was not studied further. This study concerns only those cases of paroxysmal tachycardia in which there were definitely dropped ventricular beats.

Race, Sex, Mortality.—Table I shows the insignificant sex and racial distribution, as well as the significant mortality statistics. Death occurred in twenty-two cases (55 per cent) during the period of hospitalization in which paroxysmal tachycardia with block was found. This fact emphasizes the serious prognostic implication of the concomitant presence of A-V block and paroxysmal tachycardia.

TABLE I

SEX, RACE, AND MORTALITY

	WHITE MALE	WHITE FEMALE	COLORED MALE	COLORED FEMALE	TOTAL
LIVED	6	4	6	2	18 (45%)
DIED	7	3	8	4	22 (55%)
TOTAL	13	7	14	6	40 (100%)
	Males 27 (67.5%)			Females 13 (32.5%)	

TABLE II

TYPE OF HEART DISEASE

AGE (DECADE)	NO HEART DISEASE	CONGENITAL	SUBACUTE BACTERIAL ENDOCARDITIS	POST PARTUM	SYPHILITIC	HYPERTENSIVE	ARTERIOSCLEROTIC	HYPERTENSIVE AND ARTERIOSCLEROTIC	TOTAL
10-19		1							1
20-29	2		1	1					4
30-39					1	2			3
40-49						7	2	1	10
50-59								6	6
60-69					1	3	3	2	9
70-79							1	4	5
80-89					1			1	2
Total	2	1	1	1	3	12	6	14	40
							32		

Type of Heart Disease.—Table II shows the distribution according to age and according to the etiologic type of heart disease. The heart was normal in only two cases. One patient had a congenitally hypoplastic aorta with cardiac failure; one had subacute bacterial endocarditis, probably engrafted on rheumatic valvulitis; one had fatal myocardial failure three weeks post partum; three had syphilitic aortitis with aortic regurgitation. The remaining 32 patients (80 per cent) had either hypertensive or arteriosclerotic heart disease; the two were usually, but not invariably, associated. In thirty-five of this series congestive heart failure was present before the appearance of the paroxysmal tachycardia

TABLE III

TABULATION OF THE VARIOUS ATRIAL RATES AND THE GRADE OF A-V BLOCK IN THE INDIVIDUAL CASES

CASE NO.	ATRIAL RATE	GRADE OF BLOCK	CASE NO.	ATRIAL RATE	GRADE OF BLOCK	CASE NO.	ATRIAL RATE	GRADE OF BLOCK	CASE NO.	ATRIAL RATE	GRADE OF BLOCK
1	174-179	1:1	12	200	5:4, 4:3 W	22	207	1:1	31	162	6:5 W
	187-190	4:3, 3:2 W					222	3:2 W			CSP 4:1, 6:1
			13	125			255	2:1			
2	184-192	2:1		Node 165	Complete				32	150-160	2:1, 3:2
						23	196	1:1			
3	272	6:4, 5:4, 4:3 W	14	182	8:7, 7:6 and less		Prostig. 182	2:1	33	156	2:1, 4:1 with vent. esc.
							Resp.				
				193	Rare		156-176	2:1, 3:1			
4	158	2:1							34	150	3:2, 6:5 and less
	187	2:1	15	187-190	1:1	24	171-179	2:1, 3:2W			
	190	2:1		102-105	3:2 and less W						
	194	2:1				25	167	1:1, 12:11 W	35	193-207	3:2, 2:1
		CSP 3:1, 4:1	16	162	1:1		182	4:3, 3:2, 2:1 W			
				Deep resp.					36	171-193	3:2, 2:1, 3:1
5	250-255	2:1		144-150	5:4, 2:1 W		196	2:1			
				CSP	2:1, 6:5 W				37	207-214	2:1
6	164-187	6:5, 9:8, 23:22 W		Quinidine		26	260	2:1, 3:1			
				143-158	3:1 with vent. esc.				38	158	6:5 and less
						27	214	1:1			
7	273-286	2:1	17	158-164	1:1		200	2:1	39	154	3:2
				214-240	1:1			CSP 3:1 with			
8	182	1:1		160-169	4:3, 11:10, and less W			Resp. vent. esc.	40	194-214	5:4, 8:7 and less
	200-203	4:3, 3:2 W									
			18	150-188	2:1, 9:8, 8:7 W	28	184-197	13:12, 9:8, 6:5, 2:1 W			
9	125	1:1									
	143	8:7, 3:2 W	19	190	4:1 with vent. esc.						
						29	179-190	2:1			
10	179	2:1	20	167	1:1						
				179	5:4, 3:2 W	30	230-240	2:1			
11	169	1:1									
	190-218	5:4, 3:2 W	21	222	1:1						
				118	7:5						

The presence of the Wenckebach type of block is indicated (W). The effects of carotid sinus pressure (CSP), of deep respiration, of prostigmine, and of quinidine are recorded in certain instances. Ventricular escape occurred with the higher grades of block. The grade of block is sometimes proportional to the atrial rate, e.g., Case 22; more often, factors other than the atrial rate seemed to determine the degree of A-V block.

with A-V block. In two instances failure was precipitated by the rapid heart action; in three cases there was no myocardial failure. Fifteen patients were studied at necropsy and in eight of these pulmonary embolism was found.

Medication.—Study of the records showed that the preceding medication played an important role both in the precipitation of the tachycardia and in the production of A-V block. Only seven patients had received no digitalis. Of the remaining thirty-three, twenty-three had an obvious overdosage of digitalis. The other ten had received what appeared to be reasonable doses, but they may have been too much for these particular patients. A history of previous digitalis administration may have been overlooked or not recorded. In these thirty-three cases, digitalis medication preceded, and may have precipitated, the tachycardia in twenty-five instances. In six cases digitalization caused A-V block in a pre-existing tachycardia; in the remaining two the block was definitely induced by prostigmine. Prostigmine was used in another case without effect.

In three cases the tachycardia with block appeared immediately after large diuresis due to mercuparin. We interpret this phenomenon as a consequence of overdigitalization resulting from diuresis. Aminophylline administration preceded the tachycardia in ten cases, in seven of which it was given by vein. In one instance the block appeared immediately after the intravenous use of aminophylline. Coramine was given to three of the patients, but we cannot say that it contributed to the development of tachycardia, either with or without block. Quinidine was given to six patients, and may well have contributed to the impaired A-V conduction.

The grade of A-V block varied somewhat. The most common type was 2:1, which was recorded in twenty-one patients. Progressive increases (Wenckebach periods) occurred in twenty-two cases. There were 4:3 and 3:2 in eighteen electrocardiograms, with lower grades of 5:4 to 10:9 in fifteen, and still lesser grades in six. Nine patients, on the other hand, developed higher grades of block: 3:1 was recorded six times, 4:1 four times, and 6:1 once.

Increased conduction disturbances were produced by carotid sinus pressure in four electrocardiograms, whereas respiratory changes increased the block in two cases and change of position produced this in one instance. There were other electrocardiographic abnormalities of note. The intraventricular conduction time was increased during the paroxysm in eight cases.

The P-P cycle length showed alternation in nine instances; the cycle containing the ventricular complex was shorter than the following one in which A-V conduction was blocked. This was probably due to vagal reflex inhibition of the ectopic pacemaker, similar to that demonstrated by Ashman and Gouaux[18] in complete A-V block.

TABLE IV

Grades of Block

6:1	1	4:3, 3:2	18 cases
4:1	4 } 9 cases	5:4 to 10:9	15 cases
3:1	6	Less	6 cases
2:1	21 cases	Wenckebach type of block	22 cases

Carotid sinus pressure increased block	4 cases	
Respiratory change increased block	2 cases	
Postural change increased block	1 case	
Delayed I-V conduction during paroxysms	8 cases	
P-P cycle change with block	9 cases	
Pulmonary embolism and infarction	8 cases	(15 necropsies)

Auricular Rate and Grade of Block

RATE	NO. OF CASES	GRADE OF BLOCK
<150	3	rare block → 3:1
150-199	26	rare block → 6:1
200-249	9	5:4 3:1
>250	5	5:4 3:1

Associated Atrial Mechanism Disturbances

	BEFORE A-V BLOCK	AFTER	INDIVIDUAL CASES TOTAL
Atrial paroxysmal tachycardia	11	6	12
Atrial premature beats	7	7	10
Atrial fibrillation	6	4	9
Atrial flutter	1	3	4
Shifting pacemaker	2	1	3
Delayed A-V conduction	1	2	2

TABLE V

MEDICATION
(AS CONTRIBUTING FACTOR TO TACHYCARDIA AND BLOCK)

DIGITALIS	CASES			CASES
None	7		Produced block in pre-existing tachycardia	6
Moderate doses	10 } ↔ 33		Produced both tachycardia and block	25
Overdosage	23 }		Produced tachycardia; block produced by prostigmine	2
MERCUPURIN	3		PROSTIGMINE	2
QUINIDINE	6		CORAMINE	3
AMINOPHYLLINE	10 (7 i.v.)			

HEART FAILURE	
Absent	3
Induced by tachycardia	2
Present before tachycardia	35

Associated atrial mechanism disturbances were present in many cases before and after the time during which A-V block was recorded. Other attacks of uncomplicated paroxysmal atrial tachycardia antedated the block attack in eleven cases and postdated it in six cases in twelve patients. Atrial premature beats were recorded before the block attack seven times and after it seven times in ten patients. Atrial fibrillation was present in six instances preceding the paroxysmal tachycardia with block, and, subsequently, four times in nine patients. Flutter was

present one time before, and three times afterward, in four patients. Delayed A-V conduction had been present in two earlier electrocardiograms and occurred in one instance in the later electrocardiogram in two patients. A shifting pacemaker was recognized in two patients before the paroxysmal tachycardia with block attack, and once afterward.

DISCUSSION

It must be explicitly stated that we do not possess absolute criteria for sharp differentiation between atrial tachycardia and flutter. We have set down the criteria which have guided us, the most basic of which is the presence or absence of an isoelectric mechanism. Even this may not be valid, for a circus mechanism has been postulated for tachycardia.[19, 20] We do not propose to discuss this possibility further at this time, for we have excluded from this series several instances in which paroxysmal tachycardia was closely associated with definite flutter or fibrillation, and are studying this association further. In our opinion, the cases illustrated conform to the criteria cited, although it is certainly desirable to obtain more absolute criteria for sharper differentiation.

In studies that are among the earliest of electrocardiographic-pharmacologic experiments, Lewis, White, and Meakins[21] showed that the atrioventricular junctional tissue is most susceptible to influences which depress conduction. Lewis, Drury, and Iliescu[22] found that among the influences that produced block were asphyxia, increased atrial rate, vagal stimulation, and strophanthin. Local increases in hydrogen-ion concentration have been found to have a similar effect. Our observation that A-V block occurs rather frequently in paroxysmal atrial tachycardia, particularly in hearts that are affected by myocardial disease, or which have been subjected to digitalis or quinidine medication, is merely clinical confirmation of these older experimental observations. Wilson and Wishart[23] comment on the rarity of block in paroxysmal tachycardia, as compared to its frequency in flutter, but refer to one instance of their own in which digitalis and added vagal tone did induce block. They also illustrate a case in which two paroxysms terminated with blocked atrial complexes.

Tachycardia of the type under discussion occurs commonly in normal hearts. However, only two hearts of the present series could be called normal (Cases 6 and 21). In Case 6 the patient had been given moderate doses of digitalis, and in Case 21 he had received an obvious overdosage. In other words, every patient included in this study had either myocardial disease, coronary or aortic disease conducive to myocardial anoxemia, or had received digitalis. In two instances the vagotonic effect of prostigmine was an added factor in producing A-V block. Most of the patients had disease of the myocardium and had received, *in addition,* digitalis, quinidine, or both. In our experience, such influences produce A-V block not uncommonly, although its appearance in normal hearts is distinctly rare.

The high incidence of A-V block among our records of paroxysmal tachycardia is probably due to the fact that most of the records were obtained from patients who had been hospitalized for cardiac disease. In fact, the majority of them had disease extensive enough to have led to congestive heart failure.

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THE NORMAL HUMAN VENTRICULAR GRADIENT

III. The Relation Between the Anatomic and Electrical Axes

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IN THE first paper of this series[1] we presented the results of our study of the directions of the QRS axis and QRS-T axis, with reference to their projection on the frontal plane of the body, and the relation between the axes as these were influenced by apparent rotation of the heart about anteroposterior, transverse, or longitudinal axes. We also examined certain normal influences which seemed to cause a change in the relation between the axes. In the second paper[2] we inquired into the manifest magnitudes of the QRS (A_{QRS}) and QRS-T (G) vectors, the projections of the spatial vectors, $S\hat{A}_{QRS}$ and $S\hat{G}$, upon the frontal plane, and into the factors which affected those magnitudes. We were able to demonstrate that the magnitude of the manifest QRS area (A_{QRS}) was chiefly influenced by physical causes, namely, changes in the position of the heart within the thoracic cage, whereas the manifest area, G, or the ventricular gradient, was increased or decreased not only by the same factors which changed the manifest magnitude of the QRS area, but also by physiologic conditions, such as changes in the heart rate and, perhaps, in the ventricular stroke volume. In order to make clear the reasons for the effect of changes in position, it was necessary to anticipate the material of the present paper. Although extended discussion was avoided, it was stated that we were mainly concerned with three axes, namely $\hat{A}_{QRS}$, $\hat{G}$, and a longitudinal anatomic axis around which the heart could rotate. This paper will describe these three axes, together with the anteroposterior and transverse axes of rotation, and will define, with the evidence, the spatial relations of the first three.

1. *Anatomic and Physiologic Considerations.*—The cardiac ventricles are located in the thoracic cavity and rest upon the diaphragm. In the average cardiac position, the atrioventricular valve openings are somewhat above and to the rear; the cardiac apex is somewhat below and near the anterior thoracic wall. As viewed from the front, the anterior surface of the ventricles is largely right ventricular wall, and a larger or smaller extent of left ventricular surface is visible to the left of the interventricular groove. If there is clockwise rotation of the heart about a long axis, less of the left ventricular surface is visible; if there is counterclockwise rotation, more of that surface is seen. In most hearts, the whole right border, from the root of the superior vena cava or aorta to the diaphragm, is formed by the right auricle. In other hearts, a

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small part of the right ventricular border is visible between the diaphragm and the right auricular border. Because of these differences it is likely that no method of ascertaining the long axis of the ventricles is quite accurate, and for convenience we have chosen the line drawn from the aortic-atrial angle to the ventricular apex as the longitudinal anatomic axis.

On excitation, the ventricles presumably are activated by impulses delivered by way of the bundle branches and their subdivisions. Since we are dealing with the axes as they are recorded or calculated, rival theories of the mode and sequence of ventricular excitation do not concern us. The facts of animal experimentation, of which the latest and probably the most useful study is that of A. Sidney Harris,[3] demonstrate that the epicardial surface of the anterior, apical, right and, in part, anterior left ventricular walls is the first to become fully activated in the monkey. The left ventricular base and the pulmonary conus are latest. In the dog and cat the time relations are similar, although not identical. This may readily be interpreted as meaning that the *instantaneous* electrical axis of QRS initially points forward and downward. But this direction is not long maintained. The instantaneous axis rapidly rotates, to right or left, and comes to point more or less backward, and finally even upward, in most hearts. The relatively backward direction, being longer maintained, causes the *mean* axis of the QRS to point in a backward direction relative to the anatomic axis. A paper by Gardberg and Ashman[4] considers in detail the electrocardiographic consequences of this upon the instantaneous electrical axes which compose the QRS complex.

After inscription of the QRS complex, the RS-T segment and T wave are written. The repolarization of the muscle has begun in the regions earliest to enter into activity before the activation of the whole muscle mass is complete. Hence, any displacement of the S-T segment, not due to disease, is considered to be a part of the T complex. Repolarization of the ventricles, as explained in our first paper, occurs in general in a direction which differs from the order or sequence of depolarization. In other words, the orders of accession and regression are not the same.[5] This is the reason for the existence of the ventricular gradient, and, as a matter of fact, the orders of accession and of regression are nearly opposite, under usual, normal conditions. It is most convenient to assume that the subepicardial muscle fibers, in general, recover more promptly than the subendocardial fibers, and it may eventually be found that the major effects in the production of the gradient are within the left ventricular walls, including the septum.

Since the mitral and aortic valve openings cannot participate in this, the unbalanced electrical forces are directed approximately, although almost certainly not precisely, opposite the valve openings. If all the left ventricular walls shared equally in producing the effect, and the

right ventricle not at all, the axis of QRS-T ($\hat{G}$) would then point from the center of the combined valve openings on the left, out through the wall opposite the openings. To the extent that the position of the heart shifts during systole, will the direction of the electrical forces then produced experience a change in direction. It appears possible that the leftward shift of $\hat{G}$, which was stated to occur under some, although not under all, conditions of cardiac acceleration, is due to this.

Our present problem is to ascertain the *apparent* directions of the mean spatial QRS ($S\hat{A}_{QRS}$) and QRS-T ($S\hat{G}$) axes, relative to each other, and relative to the anatomic axis.

2. *Materials Used.*—These were the same as those described in the second paper of this series. In addition, orthodiagrams or roentgenograms were obtained on eighteen subjects, and measurements were made of the anteroposterior chest diameter at the level of the fourth intercostal space at the sternum, together with measurements of the transverse thoracic diameter at the level of the cardiac apex. With the permission of the author and the publishers, we have also made extensive use of the excellent roentgenograms and electrocardiograms in Master's book.[6]

3. *Estimation of the Size of the Angle Between the Mean Spatial QRS ($S\hat{A}_{QRS}$) and QRS-T ($S\hat{G}$) Axes.*—In the first paper, it was shown that when the ventricles are rotated in a clockwise direction around the longitudinal axis of rotation, $\hat{A}_{QRS}$ lies to the right of $\hat{G}$, and it was shown that counterclockwise rotation causes $\hat{A}_{QRS}$ to lie to the left of $\hat{G}$. It was pointed out that this can only mean that the directions of the two axes are different and that the spatial axis, $S\hat{A}_{QRS}$, points backward relative to the spatial axis, $S\hat{G}$. But it is apparent that the angle between $S\hat{A}_{QRS}$ and $S\hat{G}$, the ventricular gradient, is not correctly reflected in the projection of these axes on the frontal plane. Reference to Fig. 1 will make it easy to see that when the QRS axis is directly behind the QRS-T, their directions relative to the frontal plane will be the same. On the other hand, if the longitudinal axis of rotation (H) were in the frontal plane, and if the heart were rotated sufficiently about the H axis, either clockwise or counterclockwise, both axes would come to lie in a plane parallel to the frontal plane, and the angle between them would be the true angle. At the same time the manifest areas would be at their maximum.

a. In order, therefore, to attempt to ascertain the true size of the angle, we may select those few cases which show nearly maximum net QRS areas, and nearly maximum QRS-T areas for the heart rate. The true angle should be no smaller than the recorded angle, although it will probably be larger, since the required rotation may not normally occur, and the axis of rotation will not often be in the frontal plane. Furthermore, since we have found that normal, counterclockwise rotated hearts do not show maximal QRS and QRS-T areas in our series of cases, we may confine our search to hearts with clockwise rotation. We must not forget, also, that unavoidable error in measurement may give us

angles which are several degrees too large or too small. The result of this method shows that the four largest angles, directly recorded, are 19, 20, 22, and 23 degrees, respectively. Allowing for error, the angle between the QRS and QRS-T axes is, therefore, greater than the average of those figures, or 21 degrees. The larger angles seen in Fig. 2 of the first paper can be ascribed to foreshortening of the angle as projected upon the frontal plane, and possibly to change in position of the heart during systole.

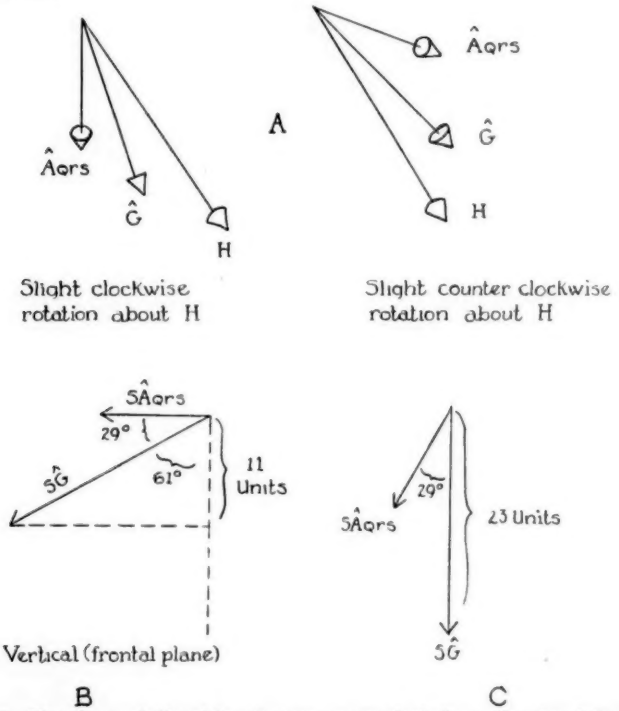

Fig. 1.—*A*, Showing relationship of axes as projected on the frontal plane, with clockwise rotation about H, on left, and counterclockwise rotation about H, on right. H points downward, forward, and to subject's left.
B, The spatial axes as seen in a right lateral view when the axes lie in a saggital plane. The vertical dotted line marks the intersection of frontal and saggital planes.
C, The spatial electrical axes after rotation of the heart so that SĜ marks the intersection of frontal and saggital planes. Described in text.

It should be said that the normal absence of extreme rotation, and absence of angles larger than 23 degrees when the areas are nearly maximum, are facts worth recording.

b. A trial and error method of ascertaining the size of the spatial angle between $S\hat{A}_{QRS}$ and $S\hat{G}$ was the one we first employed. Using a model showing the longitudinal axis of rotation, H, and the two electrical axes, the several axes can be drawn on the roentgenogram and the sizes of the angles chosen to give the best fit of all three axes (Fig. 1). Proceeding in this fashion, we arrived at an angle between the two electrical axes, $S\hat{A}_{QRS}$ and $S\hat{G}$, of about 31 degrees, and an angle of about 59 degrees between H and $S\hat{G}$.

c. The third method will be clearer if we refer to the axes as shown in Fig. 1, *B* and *C*. These diagrams show the $S\hat{A}_{QRS}$ and $S\hat{G}$ axes as they would appear if seen from the right side of the body. In *B* of the figure, $S\hat{A}_{QRS}$ points directly backward, so that its net area, as projected on the frontal plane, is zero. From the slope of the highest G values at different magnitudes of A_{QRS}, in Fig. 2 of our previous paper, it may be inferred that when A_{QRS} is zero, the maximum G value is about 11 units (44 microvolt-seconds). We may now imagine that the axes are rotated about a transverse axis to the position shown in Fig. 1 *C*. $S\hat{G}$ is now parallel to the frontal plane, and its projected value, G, is now at its maximum. In the previous paper, we found this maximum value to be 23 units. These data, 11 units and 23 units, enable us to calculate the angular rotation of $S\hat{G}$ as it moves from the position shown in *B* of the figure to the position in *C*. $\hat{G}$, the projected value, will grow as the cosine of the angle between it and the frontal plane. The ratio, 11:23, is 0.478. This corresponds to an angle of 61 degrees and 27 minutes, which, in round numbers, we may call 61 degrees. As is evident from *B* of the figure, 90 degrees, the angle between $S\hat{A}_{QRS}$ and the frontal plane, minus 61 degrees, or 29 degrees, is, therefore, the angle between $S\hat{A}_{QRS}$ and $S\hat{G}$, according to this calculation.

d. The fourth method of calculating the spatial angle between $S\hat{A}_{QRS}$ and $S\hat{G}$ need not be described in detail. It is obvious that when the heart is not rotated on its longitudinal axis, there will be a simple trigonometric relationship between the area, A_{QRS}, and the area, G, as the heart is rotated about its transverse axis. We found twenty-six hearts with A_{QRS} values of 3.0 units (12 microvolt-seconds) or less, including negative values. Such areas preclude much rotation on H. The average value was 1.0 unit, and the average value of G was 8.4. Another group of twenty-seven nonrotated hearts had A_{QRS} magnitudes of over 3.0 units; the average was 7.0 units, and the average value of G was 13.9. In both groups, the values were those after adjustment to a heart rate of 80.[2] If the magnitude, SA_{QRS}, is between 10 and 11 units (see below) it may be calculated that the spatial angle between $S\hat{A}_{QRS}$ and $S\hat{G}$ is 29 degrees. This agrees with the third method of calculation. Although there are valid mathematical objections to averaging the values used, this method should give a fairly good approximation.

In recapitulation of the four methods of calculating the angle between the two vectors, the first shows that the angle is somewhat greater than 21 degrees; the second, as first employed, indicated about 31 degrees; and the two calculations agree on nearly 29 degrees. We will be sufficiently correct, therefore, if we take 30 degrees as the true angle in the typical normal adult heart, with the subject in the supine position.

Unless we put in an emphatic comment at this point, the third analysis given (paragraph c) may be interpreted as meaning that in actuality the heart may rotate 61 degrees about a transverse axis when different

persons are compared. The calculation does not mean this. When A_{QRS} is zero, the heart cannot be in a position of rotation on its long axis. On the other hand, the maximum G values will usually be obtained in rotated hearts. If we assume that the same heart could show the required changes, it could rotate 30 degrees on a transverse axis and 30 degrees on H to change from the position of minimum manifest mean QRS area to that of maximum manifest mean QRS-T area. Such changes, when different subjects are considered, are certainly not extreme.

The Magnitude of the Mean Spatial QRS Vector.—We may now, in passing, attempt a rough, indirect calculation of the true magnitude of SA_{QRS}. Again referring to Fig. 2 of the previous paper,[1] we find that the average value of A_{QRS}, when G was 23 units, was about 9.5 units. After allowing for the fact that most of these hearts were somewhat rotated, that A_{QRS}, although large, could not have been quite at its maximum magnitude (since no heart in a normal chest can be strongly enough rotated to bring all three axes into the frontal plane), we may guess, trigonometrically, that A_{QRS}, the projection of SA_{QRS}, has about 85 or 90 per cent of the average magnitude of the latter when G is 23 units, and that the average of SA_{QRS} is, therefore, about 10.5 or 11 units, although it may possibly be somewhat larger. Since the persons in question were men, this may be regarded as the approximate average SA_{QRS} in that group. It is noteworthy that only eight A_{QRS} values in 270 subjects exceeded the value of 10.5 units, and that seven values lay in the range 10.4 plus-minus 0.1 units. No doubt, with respect to the values both of SG and SA_{QRS}, there is some individual variation. A few of our highest A_{QRS} values may, of course, be abnormal, particularly the four cases at 11.9 to 12.6 units, assuming their size was not overestimated. When a patient is found to have a large, carefully measured A_{QRS} (we may call 11 units the upper limit of the normal), it is obvious that the case should be analyzed to decide whether the large value is due to the position and rotation of the heart, or to changes produced by disease. This, of course, is also true of very small A_{QRS} values. Because of the narrowness of the QRS complex in young children, there can be no doubt that their average SA_{QRS} magnitude is considerably smaller than that of adults.

Our data may, of course, be subjected to further analysis of a mathematical type. For example, when the A_{QRS} values are negative, and the axis lies in the neighborhood of minus 110 degrees, the manifest mean area of QRS-T should be near the minimum, on the average. This agrees with the observed facts of our few such cases. The maximum values should, in general, be observed in hearts rotated rather strongly in a clockwise fashion which are not vertical, and this again is distinctly in accordance with the observed facts. These observations afford further evidence that the two axes are separated by an angle of fair magnitude,

and that rotations of various types and degrees are reflected with consistent faithfulness by the electrocardiogram. This statistical analysis, however, gives us no direct information regarding the angles between the electrical axes and the longitudinal axis of rotation, although this might be inferred, nor does it tell us the extent to which individual hearts may deviate from the averages. Many hints suggest that the latter divergences are not great. We will now proceed to a comparison of the electrocardiographic with the anatomic evidence. This should give us further information along the lines we have considered.

4. *The Size of the Angles Between the Several Axes, Estimated From a Comparison of the Electrocardiogram and the Cardiac Silhouette.*—As a preliminary to this study, by use of a model of the electrical and anatomic axes, we compared the directions of $\hat{A}_{QRS}$ and $\hat{G}$, as shown by the electrocardiogram and the anatomic axis as shown by the roentgenogram. With the permission of the author and the publishers, we have drawn the silhouettes and thoracic outlines shown in our Figs. 2, 3, 4, and 5 from A. M. Master's valuable and instructive book,[6] so that these are available to the reader who may be interested in checking our observations against a reliable series of roentgenograms and electrocardiograms. To this series, we have added eighteen cases of our own. We may note here that our analysis fully vindicates Master in his insistence upon the importance of positional changes of the heart.

In our study of Master's figures, after a good bit of trial and error, we finally devised a model which had a 90 degree angle between the longitudinal anatomic axis of the heart and the mean QRS axis, and a 59 degree or 60 degree angle between the anatomic axis, H, and the ventricular gradient, the three being in the same plane (Fig. 1 *A*). The model was attached, by the lower end of its H axis, to a rubber ball, so that it could be rotated in front of a chart. The α angles were marked on the chart as radiating lines, and concentric circles were drawn around the center of radiation so that the net manifest mean area of the QRS complex (A_{QRS} values) could be represented. A source of light, nearly 30 feet distant and properly placed, projected the shadow of the model upon the chart. The model was then adjusted so that H on the model coincided with the direction of H shown by the cardiac silhouette. Keeping H fixed, further adjustments and rotations were made until the direction and the magnitude of $\hat{A}_{QRS}$ were also correct for the heart being studied. The direction of $\hat{G}$ was then read from the chart, and this direction is called the "calculated" $\hat{G}$ (Tables I and II), which is then compared with the actual direction of $\hat{G}$ as it was ascertained from the electrocardiogram. If, in the whole series of cases examined, the "calculated" and actual directions of $\hat{G}$ are in good agreement, it may then be assumed that the angle between $S\hat{A}_{QRS}$ and $S\hat{G}$ chosen for the model is nearly the same as the true spatial angle. At the same time, the tables show the range of variation in axis directions in normal subjects. As

will be shown, if the electrocardiogram indicated clockwise or counterclockwise rotation, then in nearly all instances it was necessary to rotate the model in the corresponding direction to obtain a good agreement between the axes. In most instances, when the electrocardiogram showed that the apex should be tilted forward or backward, it was found that this movement resulted in better agreement between the calculated and observed relations. It will be seen that, since there were five

TABLE I

SUBJECT NO.	AGE AND SEX	AREA A_{QRS}	ROTATION *	H (DEGREES)	$\hat{A}_{QRS}$ (DEGREES)	$\hat{G}$ (DEGREES)	CALCULATED $\hat{G}$ (DEGREES)	DISCREPANCY, TO RIGHT OR LEFT OF CALCULATED (DEGREES)
4	10 mo. F	3.70	c5	+26	+74	+66	+56	10 R
5	5 F	5.20	c4	+39	+88	+63	+61	2 R
6	7 M	7.65	c4	+42	+97	+76	+77	1 L
7	12 M	7.60	c3	+48	+88	+69	+72	3 L
8	20 F	4.10	c1	+38	+68	+46	+51	5 L
9	30 M	5.75	cc2	+35	- 5	+15	+16	1 L
10	60 M	4.65	cc3	+35	- 5	+16	+19	3 L
11	75 F	7.30	cc5	+36	-34	- 8	- 2	6 L
12	81 M	6.70	cc5	+33	-28	- 9	+ 3	12 L
13 *A*	21 M	6.90	c3	+32	+42	+28	+38	10 L
13 *B*	21 M	8.20	c3	+43	+82	+67	+68	1 L
14 *A*	44 F	5.60	c2	+50	+77	+74	+65	9 R
15 *A*	73 M	4.30	cc3	+42	+20	+44	+32	12 R
15 *B*	73 M	3.70	cc2	+44	+54	+64	+48	16 R
16 *A*	12 M	8.35	c2	+30	+52	+42	+46	4 L
16 *B*	12 M	6.50	c3	+44	+83	+64	+66	2 L
17 *A*	12 F	2.60	c1	+34	+74	+39	+42	3 L
17 *B*	12 F	2.60	c1	+33	+74	+19	+42	23 L
18 *A*	27 F	7.75	cc3	+38	+18	+12	+25	13 L
20 *A*	29 M	2.00	cc1	+33	+25	+38	+29	9 R
21	45 M	6.30	c2-3	+43	+77	+69	+63	6 R
23 *B*	35 M	6.00	c3	+56	+92	+68	+73	5 L
24	21 M	7.40	c3	+54	+95	+81	+73	8 R
22†	15 M	4.50	cc2	+56	+50	+56	+54	2 R
25	26 F	8.10	c3	+46	+68	+42	+58	16 L
26 *B*	49 F	3.30	cc4	+26	-41	+ 1	+ 2	1 L
27	21 M	4.70	cc4	+30	-10	+11	+12	1 L
28 *A*	25 F	8.70	None‡	+25	+30	+24	+28	4 L
29 *A*	33 F	5.40	cc1	+26	+13	+22	+20	2 R
29 *B*	32 F	5.20	None	+35	+32	+32	+33	1 L
31	52 M	9.20	cc4	+35	-24	+ 5	- 5	10 R
36	56 F	6.20	cc2	+38	+10	+20	+22	2 L
37	29 F	9.00	cc3	+46	+29	+31	+36	5 L
42	39 M	6.10	c1	+45	+59	+54	+51	3 R
44	27 F	6.80	c3	+47	+87	+64	+65	1 L
63 *A*	34 M	7.20	c1	+45	+65	+61	+58	3 R
73	13 M	8.00	c5	+47	+120	+81	+80	1 R
78	20 F	4.30	cc4-5	+60	+23	+50	+46	4 R
84 *C*	22 M	7.00	c3	+44	+60	+43	+53	10 L
97 *B*	16 M	4.50	c2	+44	+89	+56	+60	4 L

*c = clockwise rotation on long axis as shown by electrocardiogram. cc = counterclockwise rotation. The figures 1 to 5 represent the electrocardiographic picture of very slight to doubtful rotation, 1; slight, 2; definite, 3; marked, 4; extreme, 5.

†First edition of Master's book.

‡Varies with respiration.

The fact that there are more leftward than rightward deviations of G is probably due to the fact that the electrocardiogram was usually taken with the subject semirecumbent, and the roentgenogram with the subject in a different position.

variables (the position of the three axes and the direction of rotation both about H and also about the heart's transverse axis), a good agreement, in the total series of cases, between the electrocardiogram measurements and the model cannot be due to chance. Table I gives a summary of the measurements.

We may now consider the figures from Master's book,[6] indicating in parenthesis which of our figures correspond. Although the agreement with the model appears to be good, we omit Master's 20-day-old infant, and take his figure 4, from a normal infant, 10 months old. Here A_{QRS} is rather small, although individual deflections are large, and the deep Q_3 and S_1 indicate strong clockwise rotation about H. As we measure them, $\hat{A}_{QRS}$ is plus 74 degrees, $\hat{G}$ is plus 66 degrees, and H is rather transverse, namely, plus 26 degrees. The heart rate is about 123 (average of Leads I and III). When the model was placed so that H agreed with the roentgenogram and $\hat{A}_{QRS}$ agreed with the electrocardiogram, $\hat{G}$ was about 56 degrees, differing by 10 degrees from the expected figure. It has been assumed that, in the infant, the net area of the mean QRS vector is normally smaller than in the adult because of the narrowness of the QRS complex, and correction was made accordingly. In any event, we regard the agreement as good.

It may be noted at this point that the electrocardiographic measurements, the estimation of the direction of the anatomic axis from the cardiac silhouette, and the estimate of the direction of $\hat{G}$, by use of the model, are all obviously subject to error. The electrocardiogram and roentgenogram were taken with the subject in slightly different positions in most cases. In view of these possibilities of error, the agreements shown appear to us to be very good.

In figure 5 (Fig. 2 *A*) we read $\hat{A}_{QRS}$, plus 88 degrees; $\hat{G}$, plus 63 degrees; H, plus 39 degrees. The magnitude, A_{QRS}, is nearly average. Here the model shows a $\hat{G}$ of plus 61 degrees. The expected and observed angles agree within 2 degrees, certainly far less than the errors inherent in the method. Master's figures 6 and 7 (Fig. 2, *B* and *C*) also show excellent agreement. Figure 8 (Fig. 2 *D*) shows a difference of 5 degrees, but A_{QRS} is small, increasing the probable error of the method. The electrocardiogram in this case shows a Q_1 and a larger S_1, with a trace of S_3. From the criteria in Gardberg and Ashman's paper, we judge this to be an example of slight clockwise rotation about H, and this is confirmed by the fact that the peak of R_1 is earlier than the peak of R_3. As inspection of the model will show, when the magnitude, A_{QRS}, is small, a slight rotation about H will produce a considerable angle between H and A_{QRS}. Figure 9 (Fig. 3 *A*) shows a considerable degree of counterclockwise rotation about H, and, as expected, $\hat{G}$ lies to the right of $\hat{A}_{QRS}$. The agreement between the electrocardiogram and the model is excellent. Likewise, figures 10 (Fig. 3 *B*), 11 (Fig. 3 *C*), and 12, all counterclockwise by Wilson and Johnston's vectorcardiogram[7] and by

Gardberg and Ashman's and other criteria, are in accordance with expectations, although figure 11 (Fig. 3 *C*) is from a 75-year-old woman, and figure 10 from an 81-year-old man. The latter shows a tolerable discrepancy of some 12 degrees. In Master's figure 13 (Fig. 3 *D*) there is some uncertainty regarding the anatomic axis. If it is taken as about

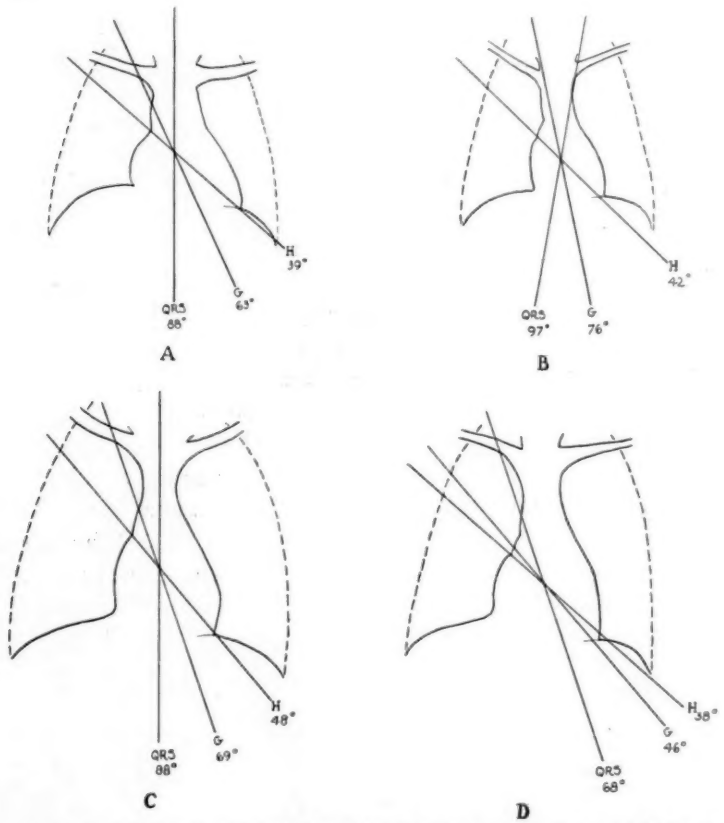

Fig. 2.—*A*, *B*, *C*, and *D* are, respectively, from figures 5, 6, 7, and 8 of Master's book.

plus 33 degrees, then the discrepancy between the actual and the expected Ĝ is about 10 degrees. Figure 13 (Fig. 4 *A*), from the same subject on deep inspiration, gives a practically perfect fit. Figures 14, *A*, *B*, and *C*, from one subject, show discrepancies of not over 9 degrees or 10 degrees; in other words, the agreement is good. Figure 15 *A* is from a 73-year-old man whose electrocardiogram shows moderate counterclockwise rotation. H is about plus 42 degrees; $\hat{A}_{QRS}$, plus 20 degrees; and Ĝ is plus 44 degrees. The magnitude, A_{QRS}, is a little below average. Here the discrepancy is about 12 degrees. Figure 15 *B* is from the same subject during deep inspiration. The electrocardiogram picture of counterclockwise rotation is less pronounced. The anatomic axis appears to be about the same as before. But $\hat{A}_{QRS}$ has rotated to plus 54

degrees and $\hat{G}$ to plus 64 degrees. The magnitude, A_{QRS}, has decreased. To obtain a fit between the model and $\hat{A}_{QRS}$ we must rotate the model slightly clockwise, opposite to the direction shown by the electrocardiogram. And $\hat{G}$ by the model is about plus 48 degrees, against the electrocardiogram measurement of plus 64 degrees. Only larger experience will show whether these two discrepancies are within the normal limits.

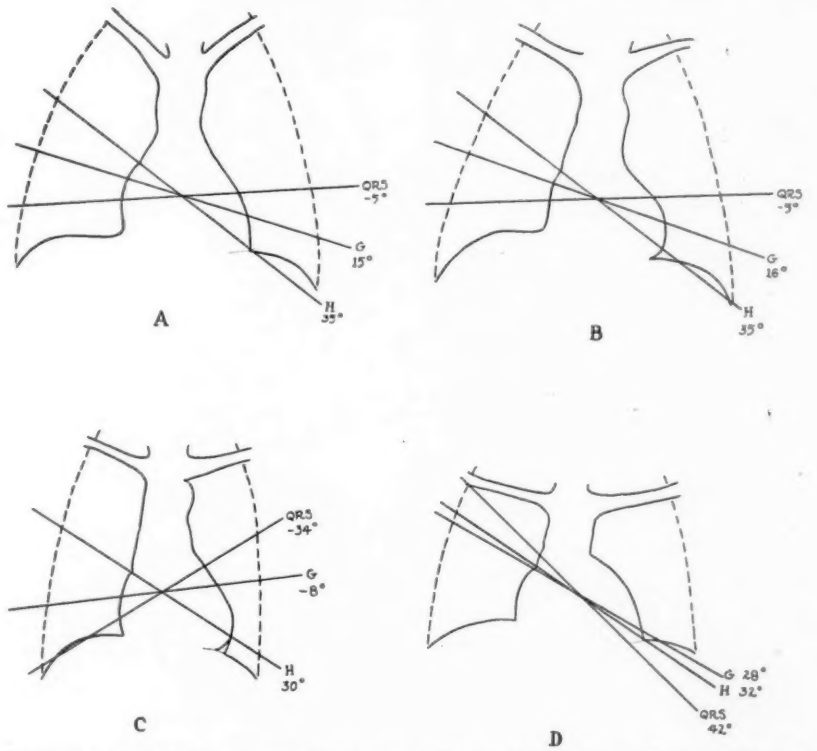

Fig. 3.—*A*, *B*, *C*, and *D* are, respectively, from figures 9, 10, 11, and 13 *A* of Master's book.

Theoretically, both changes could result from an old anterior lesion, but the rightward deviation of G may indicate emphysema, instead. The lesser counterclockwise rotation on inspiration could rotate an anterior lesion so that it would affect the limb leads. It is interesting to note that, in this case, deep respiration was required to reveal the possible abnormality.

Master's figure 16 *A* (Fig. 4 *B*), in which the electrocardiogram is interpreted as showing slight clockwise rotation, and 16 *B* (Fig. 4 *C*) (deep inspiration) show no discrepancies. Figures 17 *A* and *B*, from the same subject, show very slight clockwise rotation, as we interpret them. The small A_{QRS}, as noted above, tends to exaggerate errors. The anatomic axis in figure 17 *A* is plus 34 degrees; $\hat{A}_{QRS}$, plus 74 degrees; and $\hat{G}$, plus 39 degrees. The wide angle between $\hat{A}_{QRS}$ and $\hat{G}$ is mainly due

to the effect of "foreshortening," and G is very close to its expected position. In figure 17 *B*, in the sitting position, the H and $\hat{A}_{QRS}$ have changed little. Ĝ, however, has shifted to plus 19 degrees from plus 39 degrees. This phenomenon is not abnormal, however, as our previous papers stated. On changing the position from recumbent to sitting, and particularly to standing, the gradient usually shifts to the left, and evidently it may shift to the left of H, while A_{QRS} remains on the right, as

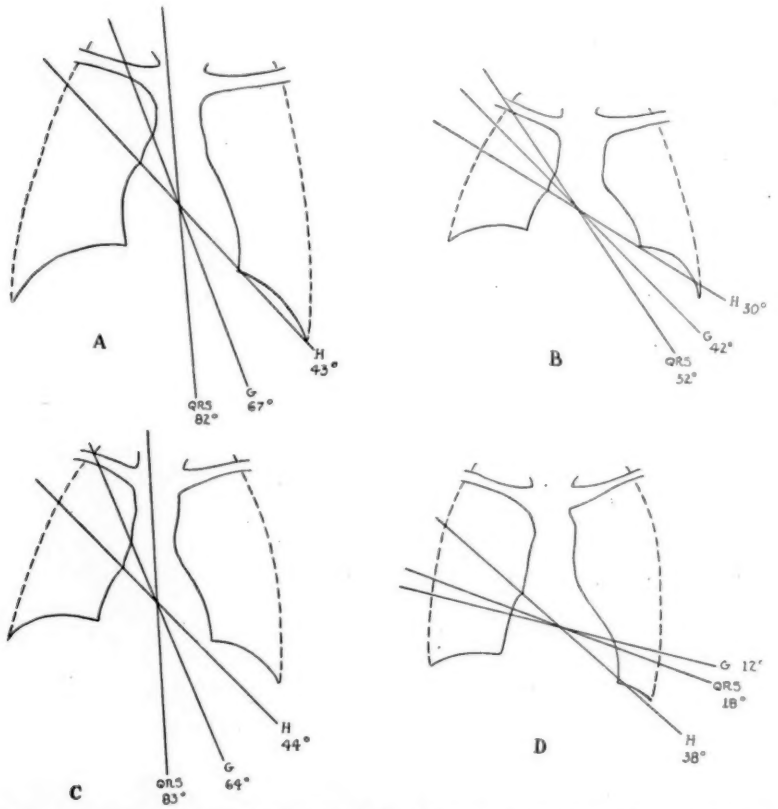

Fig. 4.—*A*, *B*, *C*, and *D* are, respectively, from figures 13 *B*, 16 *A*, 16 *B*, and 18 *A* of Master's book.

in this case. The three axes cannot now lie in the same plane. Tentatively we ascribe this effect of posture, in part, at least, to a greater change in the systolic position of the heart than occurs in the recumbent position. Figure 18 *A* (Fig. 4 *D*) shows a definite counterclockwise rotation, and the gradient is about 13 degrees farther to the left than expected. But here both a sitting position and the rapid heart may combine to produce this effect, which is normal under the circumstances. We have not attempted to measure figures 18 *B* and *C* and 20 *B* and *C*, which were taken in the lateral recumbent positions; and we also omit the abnormal records of fixed mediastinum shown in figures 19 *A*, *B*,

and *C*. Figure 20 *A* (Fig. 5 *A*) shows a discrepancy of about 9 degrees. H is plus 33 degrees; $\hat{A}_{QRS}$, plus 25 degrees; and $\hat{G}$, plus 38 degrees. $\hat{G}$ should lie at about plus 29 degrees. There is a slight counterclockwise rotation, since S_3 is larger than S_1, a small Q_1 is present, there is no Q_3, and the peak of R_3 is earlier than the apex of R_1. The net area, A_{QRS}, is exceptionally small. Figure 21 (Fig. 5 *B*) shows good agreement.

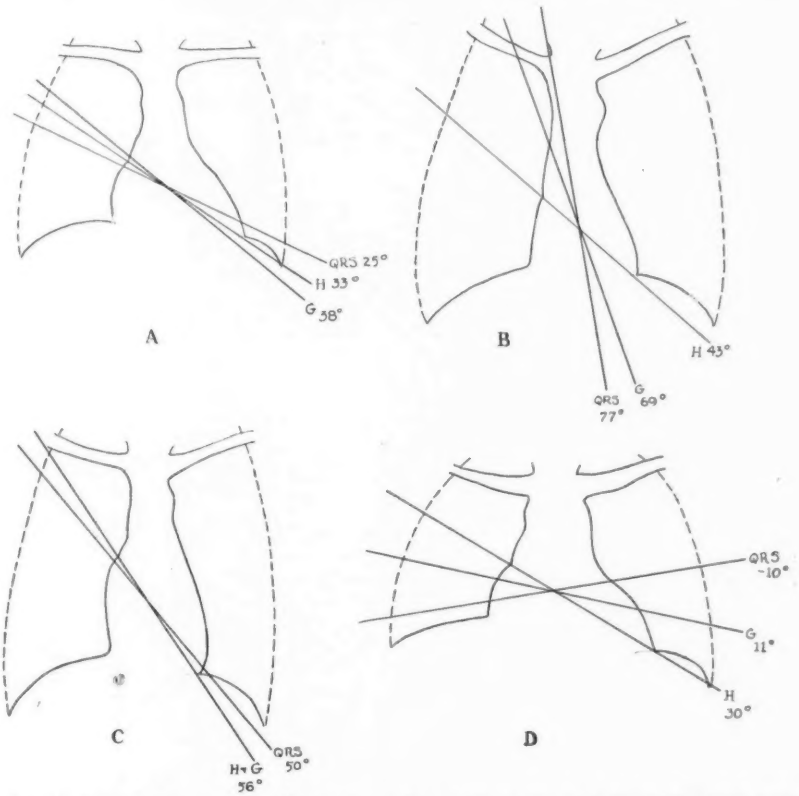

Fig. 5.—*A*, *B*, and *D* are, respectively, from figure 20 *A*, 21, and 27 of Master's book. *C* is from figure 22 of the first edition of his book.

Figure 22 illustrates the derivation of the electrical axis. Figures 23 *B* and 24 are in good accord with expectations. Our Fig. 5 *C* is figure 22 of the first edition of Master's book; it was a vertical heart, with slight to moderate counterclockwise rotation, in a 15-year-old boy, and the calculated G lies within 2 degrees of the actual one. In figure 25, the minute rate of 115, and possibly a sitting position, will account for the deviation of 17 degrees to the left of the expected $\hat{G}$ position. Here, with very little clockwise rotation, G and H are close together. Figure 26 *B* is particularly noteworthy. This obese subject, whose anatomic axis is plus 26 degrees, has an $\hat{A}_{QRS}$ at minus 41 degrees and a $\hat{G}$ at plus 1 degree. Yet the agreement is excellent, the calculated $\hat{G}$ being plus 2

degrees. Figure 27 (Fig. 5 *D*) agrees with the model: H, plus 30 degrees; G, plus 11 degrees; $\hat{A}_{QRS}$, minus 10 degrees. There is, of course, counterclockwise rotation in the electrocardiogram. Figure 28 *A* shows all the axes lying within a few degrees of each other, the rotation apparently varying very slightly from clockwise to counterclockwise with respiration. Figures 29, *A*, *B*, and *C* are from a patient who was six months pregnant. The electrocardiogram shows slight counterclockwise rotation about H, which practically disappears on deep inspiration. Agreement with the model is good. It is particularly interesting that in figure 29 *B*, as in 28 *A*, when there is little rotation, the axes all lie within a few degrees of each other, as they should. It is also noteworthy that figure 31, from a case of arterial hypertension, shows almost the normal relations of the axes: H, plus 35 degrees; $\hat{G}$, plus 5 degrees; and $\hat{A}_{QRS}$, minus 24 degrees. Figure 32, a more advanced case, with angina pectoris, shows: H, plus 25 degrees; $\hat{G}$, plus 66 degrees; $\hat{A}_{QRS}$, 0 degrees. The model will not fit this combination of axes, but it should be noted here that when the QRS complex becomes enlarged, or abnormal, the relations we describe can no longer hold. It may also be noted that some of the less advanced cases of valvular disease fit the model as well as do normal subjects.

In recapitulation, not one of the series of normal subjects from Master's book displayed any discrepancy which was not well within the

TABLE II

SUBJECT NO.	SEX	HEART RATE	AREA A_{QRS}	ROTATION (ECG) *	H (DEGREES)	$\hat{A}_{QRS}$ (DEGREES)	ACTUAL $\hat{G}$ (DEGREES	CALCULATED $\hat{G}$ (DEGREES)	DISCREPANCY, TO RIGHT OR LEFT OF CALCULATED (DEGREES)
1	M	60	4.60	c3	+31	+71	+50	+50	0
2	M	75	4.25	c4	+34	+90	+61	+53	9 R
3	M	70	1.35	cc1	+36	+30	+30	+33	3 L
4	F	84	6.00	c3	+41	+86	+55	+64	9 L
5	F	72	5.30	c2	+49	+68	+46	+57	11 L
6	M	97	6.10	c1	+34	+61	+44	+50	6 L
7	F	118	6.20	c3	+51	+90	+74	+71	3 R
8	M	114	-1.00	c1	±50	-77	+56	+49?	7 R
9	F	120	4.10	c2	+44	+82	+46	+60	14 L
10	F	63	9.05	c3	+30	+74	+58	+61	3 L
11	M	75	5.10	cc1	+33	+32	+25	+32	7 L
12	M	110	-3.50	c1?	+52	-107	+51	+40?	11 R
13	M	86	8.55	c3	+30	+58	+40	+49	9 L
14	M	120	8.30	c4	+42	+114	+86	+85	1 R
15	M	90	0.85	0	+36	+43	+20	+37	17 L
16	M	78	6.60	c3	+42	+69	+49	+57	8 L
17	M	90	4.70	c3	+42	+93	+70	+65	5 R
18	M	100	21.00†		+44	+77	+67		

*For significance of the symbols, see Table I.

†This subject had a Wolfe-Parkinson-White syndrome, with high, wide, R waves. Therefore, the QRS axis is not comparable with the normal complexes. The gradient indicates a clockwise rotation, which is what would be expected from his hyposthenic build.

Cardiac silhouette and electrocardiogram were obtained in the same position for all subjects.

limits of normal variation, as previously reported. In one case (Figure 15), indeed, deviations from the normal were noted, but the patient was well advanced in years.

In Figs. 6 to 9, we show the cardiac silhouettes and axes of sixteen persons from our own series of normal subjects. One case, which we have omitted, to save journal space devoted to figures, is an average, typical case in which there is excellent agreement between expectations

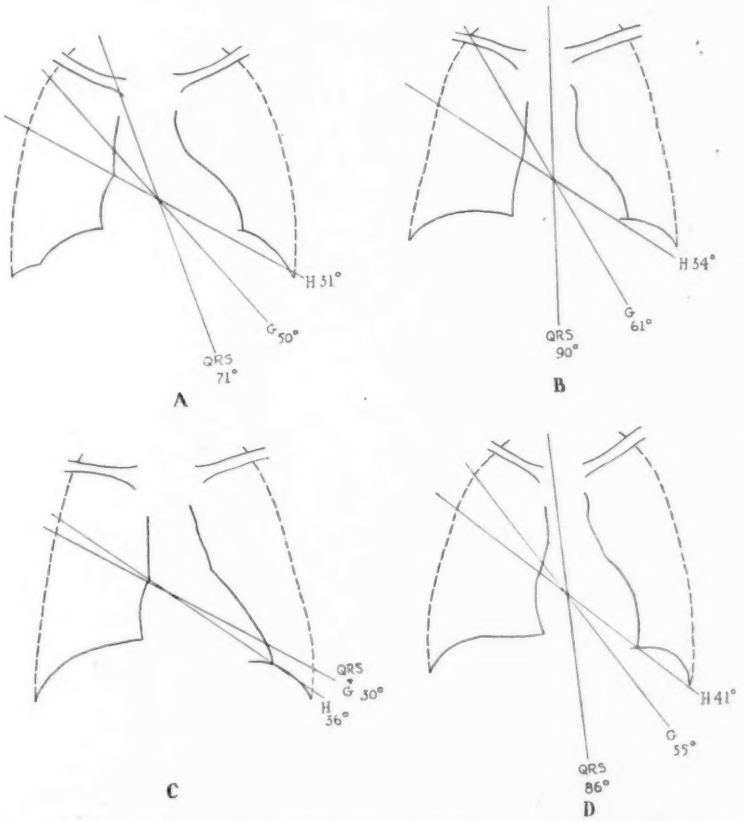

Fig. 6.—*A*, *B*, *C*, and *D* are, respectively, from roentgenograms of our Subjects 1, 2, 3, and 4 of Table II.

and predictions. The other was a case of the Wolfe-Parkinson-White syndrome, with greatly enlarged QRS complexes. In this case the heart was vertical and G was at plus 65 degrees. The orthodiagrams or roentgenograms and the electrocardiograms were taken with the subject in the sitting or standing position, as stated in the figure captions. Since the subjects were seated or standing, it is to be expected, as reported in our first paper, that the gradients will often lie farther to the left than in recumbent subjects. In order to save space, the results of this study are given in Table II.

These data require comment. It will be observed that, in six cases, the agreement between $\hat{G}$, as ascertained from the electrocardiogram, and as estimated by means of the model, is within 5 degrees, and this is true of our first omitted case. Of the remaining eleven cases, eight

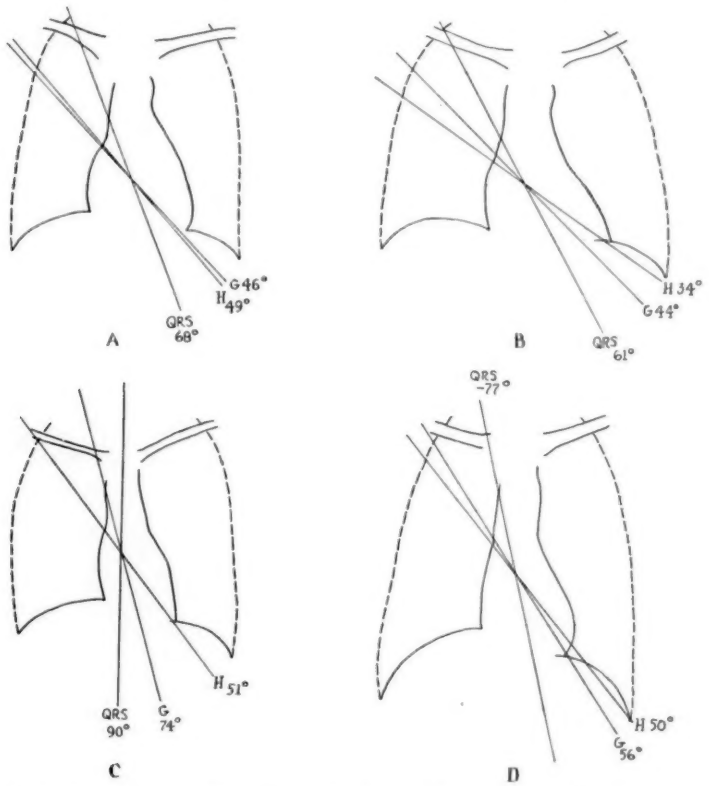

Fig. 7.—*A*, *B*, *C*, and *D* are from roentgenograms of our Subjects 5, 6, 7, and 8, respectively, of Table II.

show a deviation of $\hat{G}$ to the left of its expected direction. This is the more usual effect of the sitting or standing posture. In three cases, the gradient lay more than 5 degrees to the right of its expected position, but only Case 12 shows a discrepancy of more than 10 degrees. This was an example of a dropped heart, $S\hat{A}_{QRS}$ apparently pointing backward and upward. This subject, a medical student, had a clear history of bronchial asthma in childhood, and although the discrepancy is only about 11 degrees, it is evident that further study of such cases is required. Master's cases of emphysema show an apparently abnormal deviation of $\hat{G}$ to the right.

Since the hearts of persons with a small A_{QRS} cannot be strongly rotated, the anatomic axis, H, and $\hat{G}$ should not be widely separated, except that, as explained, $\hat{G}$ may sometimes lie even 30 degrees to the left

of its expected position when the subject stands, or even sits up. Note how this close correspondence of H and Ĝ in the nonrotated heart holds good for Master's cases 17 *A* and *B* and 20 *A*, and our subjects 3, 8, and 12. It may be noted that, as expected, most of the apparently more strongly rotated hearts do not show this close relationship between the anatomic axis and Ĝ.

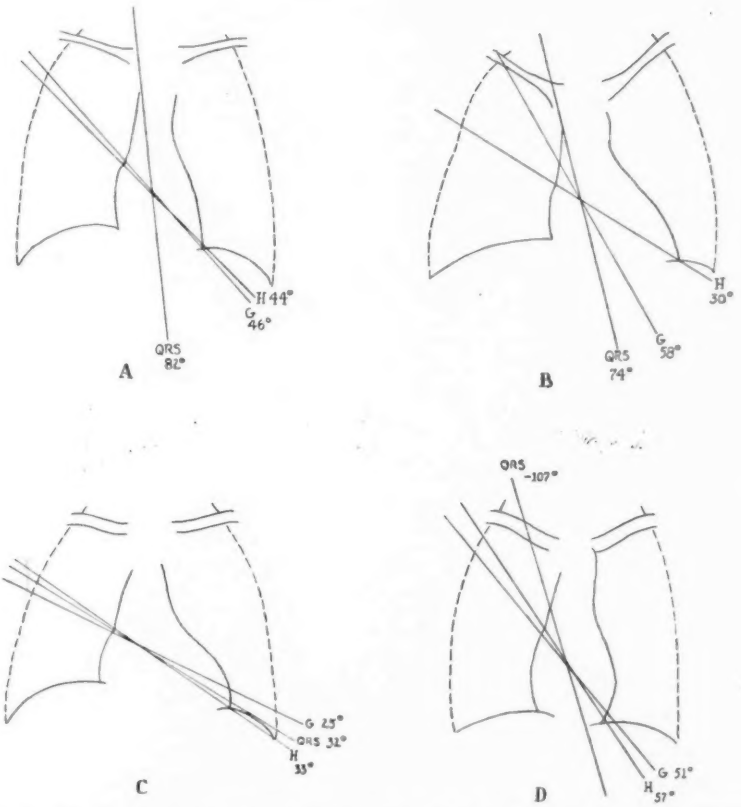

Fig. 8.—*A* and *B* are from the roentgenograms of our Subjects 9 and 10, respectively, of Table II. *C* and *D* are reduced from orthodiagrams of our Subjects 11 and 12.

Case 2 is noteworthy, since it shows that one of the more "transverse" hearts in our group has slight right axis deviation, $\hat{A}_{QRS}$ being plus 90 degrees. But this heart is apparently rotated strongly in a clockwise direction about H, as shown by a deep S_1 and a distinct, although not deep, Q_3. There was no Q_1 or S_3. In Case 9, the clockwise rotation at first seemed questionable. By construction from the electrocardiogram of the vectorcardiogram of Wilson and Johnston,[7] it was easy to demonstrate a distinct clockwise rotation which may be described as moderate. When it becomes possible to ascertain the rotation by the vectorcardiogram, to assess more accurately the effect of rotation about a transverse axis, and to ascertain the magnitudes, A_{QRS} and G, with greater pre-

cision, it is not impossible that the normal ranges of deviation between the axes will be found to be less than the methods available to us now indicate.

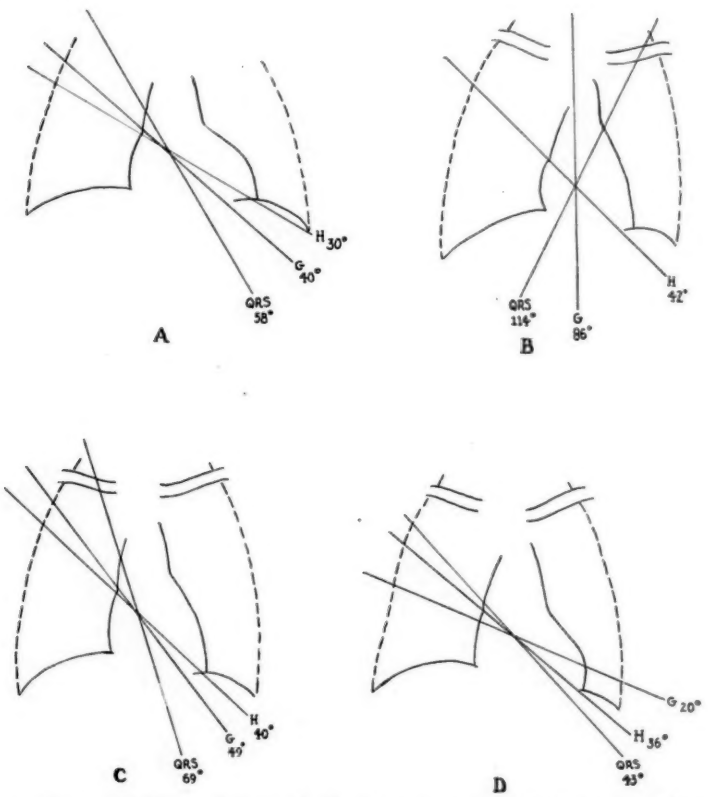

Fig. 9.—*A*, *B*, *C*, and *D* are from orthodiagrams of our Subjects 13, 14, 16, and 15, respectively, of Table II.

On the whole, however, the series is satisfactory, although the discrepancies are a little greater than in the series from Master's book. With the questionable exception of Subject 12, all fall easily within the ranges for normal subjects we have published previously. This study emphasizes the point that the electrocardiogram which is taken with the subject in the standing or sitting position may be less trustworthy than the one taken when the subject is recumbent. In a later paper we intend to publish a series of electrocardiograms, which had been interpreted as within normal limits by one of us, but which fall outside the usual range as shown by this study.

In reviewing all the normal cases of Tables I and II, it may be of interest to compare the anatomic axes and the gradients of the counterclockwise and clockwise rotated hearts. As shown by the electrocardiogram, fifteen hearts were rotated counterclockwise about H. The aver-

age anatomic axis is at plus 35 degrees, the average gradient is at plus 18 degrees, and the average $\hat{A}_{QRS}$ axis is plus 4 degrees. There are twenty-nine clockwise rotated hearts, excluding the younger children. The average H is at plus 42 degrees, the average $\hat{G}$ is at plus 57 degrees, and the average $\hat{A}_{QRS}$ is at plus 74 degrees. Although the anatomic axis of the latter group is only 7 degrees to the right of the former, the gradient is 39 degrees to the right, and $\hat{A}_{QRS}$, 70 degrees to the right. These average differences may tend to emphasize the contrast between the two groups, and to show how definitely rotation affects the direction of the gradient, and also how extreme is its effect on $\hat{A}_{QRS}$. There can be little doubt that lack of appreciation of these effects, and the apparent, although not real, discrepancy between anatomic position and the mean QRS axis have been a strong influence in the present tendency to deny the validity of the Einthoven triangle method of ascertaining the directions of the vectors. Although the fact that rotations of the heart about its logitudinal axis affect the electrocardiogram has long been known, the extent of its effects has not been generally appreciated, nor has the effect of rotation of the heart about its transverse axis been generally recognized.

5. *The Position of the Gradient (in Three-Dimensional Space) With Reference to the Ventricular Chambers.*—If we think of $S\hat{G}$, the ventricular gradient oriented in three-dimensional space, as a vector longer than the ventricles, and pointing from its electrically negative to its positive pole, we can visualize it as entering the ventricles near the margin of the right ventricular basal border, just below and to the right of the root of the pulmonary conus. It would then pass through the right ventricular chamber, and through the septum not far from its basal margin; thence it extends through the chamber of the left ventricle to emerge from that ventricle near the anatomic center of its free wall. In contrast, the QRS axis would seem to enter the ventricles a little toward the apex from the center of the free right ventricular wall, and to emerge at a point slightly toward the base from the center of the free wall of the left ventricle. Of course, the plane in which each vector lies may be in front of, or behind, above or below, the one indicated, although it seems probable that the vectors will pass through the heart not far from the center of the muscle mass. In support of the suggested three-dimensional orientation is the configuration of the QRS-T complexes observed in precordial leads (Deeds and Barnes).[8] Typically, in adults under resting conditions, the QRS complex, as recorded from the anterior surface of the right ventricle, not far from the apex, consists of a narrow, usually rather low, R wave, and a deep, much wider, S wave. The $S\hat{A}_{QRS}$ is evidently pointing away from this thoracic point, and this remains true when the area of the QRS is corrected for the potential change of the "indifferent" galvanometer contact. The QRS complex in the anterior axillary or midaxillary lead, on the other hand,

shows that the mean QRS axis points toward those thoracic regions. In contrast with the mean QRS area, is the area, QRS-T, after correction is made for the potential change at the other galvanometer electrode. At the same point over the right ventricle, the net area is positive, and this is likewise true at CF_5 and CF_6. In adults, therefore, all of these points are usually in the positive field of $S\hat{G}$. When the chest electrode is moved upward, or toward the right, however, to about the basal margin of the right ventricle, the net QRS-T area is negative. In the right axilla, and over the right scapula, for example, the area is strongly negative. This comparison of QRS and QRS-T strongly supports the conclusions drawn from a study of the limb lead electrocardiogram. The reason for the direction of $S\hat{A}_{QRS}$ is given in the paper by Gardberg and Ashman.[4] The reason for the different direction of $S\hat{G}$ must await an explanation of the physiologic or physical factors responsible for the production of the gradient. After sufficient digitalis administration, which may eliminate the gradient, the net QRS-T areas may become zero in both precordial and limb leads.

There is no need to conclude, from the foregoing facts, that the right ventricle makes any important contribution to the ventricular gradient, although that is possible. A contribution appears to be made either by the interventricular septum or by the right ventricle, or by both, however. We suspect the septum is the more important under usual conditions.

6. *The Probable Error in Vector Direction.*—One gains the impression from a comparison of such contrasting records as numbers 5, 6, 7, 12, and 23 *B* from Master's series, on the one hand, and his numbers 9, 10, and, especially, 26 *B* and 78, on the other hand, that the directions of the vectors as indicated by the electrocardiogram are substantially correct. This agrees with the conclusion of Wilson and Johnston,[7] and of Gardberg and Ashman.[4] Yet there is one conclusion we have drawn from our data, consideration of which counsels caution. This is the conclusion that the $S\hat{A}_{QRS}$ may point not only straight backward, but even backward and upward. With the data at our disposal, it is quite impossible to decide whether, as in our Case 8, from a perfectly normal male with no history or indication of either cardiac or pulmonary disease, the apparent direction of $S\hat{A}_{QRS}$ is the true one. In attempting to explain the direction of the vector, several possibilities suggest themselves.

a. The apparent upward and backward direction may be the true one, and be due to an unusually early activation of the anterior wall of both right and left ventricles, as in one of Harris' monkeys. Alternatively, an unusually large, upwardly and forwardly directed component from the pulmonary conus may produce the same effect, athough this seems unlikely.

b. The apparent direction may not be the true one. It may be supposed that, particularly for vertically placed hearts, transversely oriented vectors may have less effect on the electrocardiogram than longitudinally oriented ones for reasons which are under discussion and not understood. If, for example, the R-wave vectors point relatively transversely, they may be reduced in magnitude. If, at the same time, the S vectors point nearly vertically upward, parallel to the mediastinum, they may be little affected. The effect would necessarily be to cause an apparent upward and backward deviation of $S\hat{A}_{QRS}$. So far as we can tell at this time, a dubious effect of this sort may often cause an apparent backward deviation of the vectors, both $S\hat{A}_{QRS}$ and $S\hat{G}$; but only much further work, with adequate oblique and lateral views of the heart, will make possible an answer to this question. Whatever the ultimate answer may be for the normal thorax, we can at this time state that in pulmonary emphysema, if the heart is relatively vertical, there is often an apparent reduction in the transverse electrical components of the vectors, with a consequent lessening of the estimated spatial angle between $S\hat{A}_{QRS}$ and $\hat{G}$.

SUMMARY AND CONCLUSIONS

This study has indicated that:

1. The spatial angle separating the mean spatial QRS axis ($S\hat{A}_{QRS}$) and the ventricular gradient ($S\hat{G}$) is approximately 30 degrees.

2. The angle between $S\hat{A}_{QRS}$ and the longitudinal anatomic axis (H) is about 90 degrees.

3. The angle between H and $S\hat{G}$ is about 60 degrees.

4. When the normal subject is supine, these axes appear to lie very nearly in the same plane; but when the subject stands or even sits up, $\hat{G}$ often shows an apparent counterclockwise rotation about an anteroposterior axis, that is, it seems to deviate to the left. It may also deviate about a transverse axis, but we have no present evidence of this.

5. When the heart is definitely rotated counterclockwise on its long axis, both $\hat{A}_{QRS}$ and $\hat{G}$ lie to the left of the anatomic axis, but $\hat{G}$ lies to the right of $\hat{A}_{QRS}$. When the heart is definitely rotated clockwise, both $\hat{A}_{QRS}$ and $\hat{G}$ lie to the right of H, but $\hat{G}$ points to the left of $\hat{A}_{QRS}$ (Fig. 1).

6. In normal subjects in the supine position, the observed $\hat{G}$ should probably not deviate by more than plus-minus 15 degrees from the direction predicted from the type of rotation, the directions of $\hat{A}_{QRS}$ and H, and the magnitude, A_{QRS}.

7. In normal subjects, in the sitting or standing position, $\hat{G}$ may deviate as much as 25 or 30 degrees to the left from its predicted direction (that is, it may be rotated that much counterclockwise about an antero-

posterior axis), and tachycardia may possibly also cause similar deviation on occasion. On the other hand, in this position, $\hat{G}$ should not deviate more than 15 degrees to the right of its predicted direction.

8. When the net manifest area of QRS is small, and either positive or negative, the criteria indicated above must be applied with caution. In such cases, $\hat{G}$ normally seems to lie within less than 10 degrees of H in the recumbent subject.

9. The average magnitude in men of the mean spatial QRS vector (SA_{QRS}) is nearly 11 units (1 unit = 4 microvolt-seconds). It is probably slightly smaller in women, and it is presumably still smaller in infants and young children. (A later, mathematical calculation, made after this paper was written, indicates a true SA_{QRS} of very nearly 11.5 units in adult males.)

10. The directions of $S\hat{A}_{QRS}$ and $S\hat{G}$ are estimated in relation to the muscle masses of the ventricles.

It should be pointed out that our proposed limits are tentative. Much more work must be done before the limits can be fixed with precision for all types of subjects.

Excepting the cases of emphysematous or deformed thoraxes, or of the presence near the heart of air, fluid, or consolidations, we believe that the directions of the electrical axes, as projected on the frontal plane, are correct, probably within plus-minus 10 degrees in most cases. In this we agree with Wilson and Johnston.[7] It is suggested that, in some instances, extreme rotation of $S\hat{A}_{QRS}$ backward may be due to unusually early depolarization of the anterior ventricular walls, as in one of two monkeys studied by A. S. Harris;[3] and in other instances, pulmonary changes, perhaps even subclinical in degree, may produce a similar effect.

We are indebted to Dr. James L. Gouaux for drawing the orthodiagrams on eight of our eighteen subjects, and to Mr. W. B. Stewart and Mrs. Harriet Gregory Lawrence for preparation of the figures.

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THE NORMAL HUMAN VENTRICULAR GRADIENT

IV. The Relationship Between the Magnitudes, A_{QRS} and G, and Deviations of the RS-T Segment

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DEVIATIONS of the RS-T segment, so called, are produced usually by one of two wholly distinct mechanisms. One type of deviation or displacement is a normal physiologic phenomenon, related to the relative magnitudes of the manifest mean area of the QRS complex and of the ventricular gradient, and produced by repolarization of the muscle. The second type of deviation is never a normal phenomenon under the conditions obtaining in the human heart, and is related either to abatement, or reversal in the direction of flow, of a current of injury, or to intramuscular blocking of the wave of excitation, or to a combination of both factors.[1] Examples of this second type are usually observable in the electrocardiogram of recent myocardial infarction or of acute pericarditis. It is as yet uncertain whether the segment displacements regarded as characteristic of coronary disease, when induced in the patient by anoxia or exercise, should be classified in one or the other or in both categories, or whether it may not ultimately be necessary to include a third mechanism. This will be considered in the discussion. In any event, it is clear that no aspect of electrocardiographic interpretation is in greater need of sound theoretical analysis than the changes just mentioned. It is the purpose of this paper to analyze the first category of RS-T segment shifts. Not only is this a matter of great practical importance in itself, but, also, it is only in the light of such analyses that trustworthy interpretation of segment changes in general will become possible.

Theoretical Considerations.—One school of German cardiologists has attempted to explain the human electrocardiogram in each lead as the sum of two oppositely oriented monophasic action currents.[2] Hoff, Nahum, and their collaborators[3, 4] have recently made a similar effort. According to the latter authors, one monophasic curve represents the electrical activity of one ventricle, the other, that of the other ventricle, and the two summate to give the "bicardiogram." Quite aside from other objections to their view, it was pointed out that the interpretation of the electrocardiogram in this fashion is a serious oversimplification of the total situation.[5] But it was also stated that, as an approach to certain

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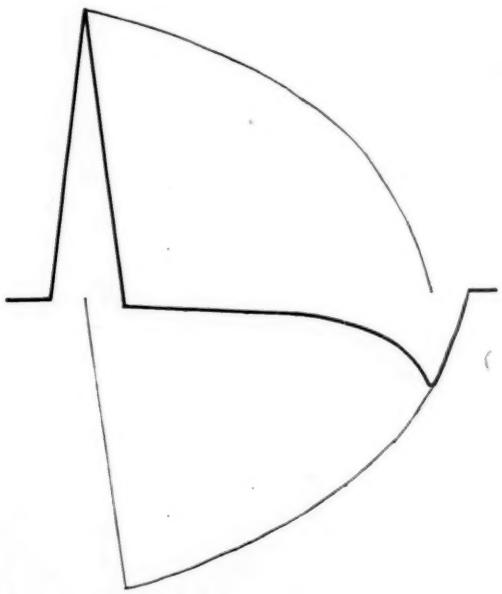
problems, the method has advantages. If used with full realization of its limitations, it affords the most easily understood approach to the problem of RS-T segment deviations of the physiologic type.

Mechanism of Production of RS-T Segment Deviation.—In Fig. 1, two monophasic curves are illustrated. The two are summed algebraically to yield the diphasic curve, consisting of the upright R wave and the downwardly directed T wave.[6] To take a specific example of what the figure may represent, let us imagine that the diphasic curve is one recorded in a precordial lead from opposite the wall of the left ventricle. Then, disregarding the right ventricle and septum, the upper monophasic curve would represent, very diagrammatically, of course, the time course of depolarization (upstroke of curve) and repolarization (downstroke of curve) of the endocardial surface of the muscular wall of the left ventricle. Since the depolarization does not involve this whole surface simultaneously, the upstroke of the curve is represented as not being very steep. The lower monophasic curve similarly represents the time course of depolarization and repolarization of the epicardial muscle surface. Its electrical effects are opposed to those of the endocardial surface, and, therefore, the direction of the curve is opposite. The lower curve begins later than the upper curve because the epicardial surface is activated later than the endocardial.

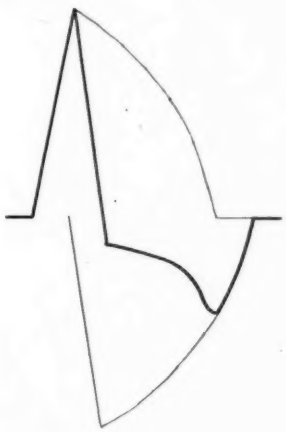


1A

Fig. 1A.—As explained in the text, the two monophasic curves of the same form, one upright and one inverted, summate to give the diphasic curve shown by the heavier line. Since repolarization of the muscle surface responsible for the upper monophasic curve has begun before the downstroke (depolarization) of the lower curve is complete, the RS-T segment is deviated downward, or "depressed." This is an example of what is called a "repolarization or regression deviation" of the RS-T segment in this paper. In this illustration, the heart rate is low.

The form of the part of each curve representing repolarization was experimentally ascertained.[7] It is a simple logarithmic curve (or very nearly so). Knowledge of its form and the effect of the heart rate upon it enable us to draw all the curves consistently. Actually, since the activation of neither muscle surface is everywhere simultaneous, the repolarization will be rather slower than as indicated, particularly at the end of the monophasic curve.

In drawing Fig. 1, it was assumed that the time course of depolarization and repolarization of the two muscle surfaces was precisely the same. As a matter of fact, in digitalized hearts, such a condition is approximated. Inspection of the diphasic curve shows a moderate *depression* of the RS-T segment. The mechanism of production of this depression is very clear. Repolarization of the subendocardial surface has gone forward before depolarization of the epicardial muscle surface is complete. This is the explanation of RS-T segment deviations of the first type, although the question as to which surfaces are actually involved is still open. In the author's opinion, this interpretation is no longer open to serious doubt.[7]



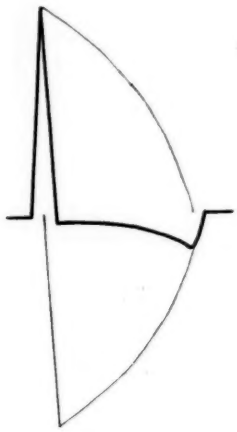
1B

Fig. 1*B*.—This is like the curve of Fig. 1*A* but it shows the effect of cardiac acceleration, which shortens the duration of the monophasic curve and increases the rate of repolarization. The differences in heights of the curves would not occur with acceleration, and is for convenience in drawing the diagrams. Note the marked increase in the "depression" of the segment, in spite of the reduction in the area of the "R wave."

Obviously, if the initial deflection, R, had been directed downward, the segment deviation would have been upward, that is, the segment would have been *elevated*. Therefore, segment deviations produced in this manner (associated, as we shall see, with a reduction in the magnitude of the gradient) are always opposed in direction to the chief initial deflection, R or S. The situation when R and S are equal is considered below.

Effect of Minute Heart Rate Upon the RS-T Segment.—In our experimental work it was shown that when the heart rate is accelerated, the

monophasic curve has a swifter descent initially; the form is close to that shown in Fig. 1*B*. Its total duration is, of course, decreased.[8] In this curve, we assume that the time required for full excitation of the surfaces, and for penetration of the ventricular wall by the impulse is the same as in Fig. 1*A*. It will be observed that the RS-T segment depression is much more pronounced after cardiac acceleration. The T wave has become deeper. Yet, as Wilson, et al.,[9] have emphasized, the area of R above the line is still equal to the area RS-T and T below the isoelectric or base line. (Since the beating heart moves with reference to the galvanometer leads between the inscription of R and T, this very precise equality would not necessarily be noted, even if one could fully eliminate the ventricular gradient.)



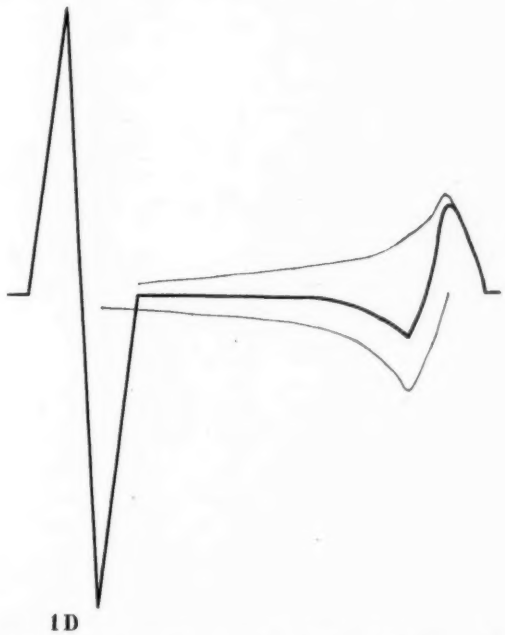
1C

Fig. 1*C*.—The height of the R wave is the same as in Fig. 1*B*, but its width is much less and its area is accordingly much reduced. Note that the RS-T deviation is only about one third as great as in Fig. 1*B*, although the rate of repolarization is the same.

Effect of Reducing the Size of the R Wave.—The effect of reducing the width, and, therefore, the area, of the R wave upon the RS-T shift and the T wave is illustrated in Fig. 1*C*, which should be compared with Fig. 2. In these latter figures, a heart rate intermediate between the other two is assumed. Since in Fig. 1*C* the area of R above the line is equal to the area of T (including the RS-T deviation) below the base line, reducing the area of R automatically decreases the area of T. And, of course, increasing R, as in Lead I in left bundle branch block, automatically increases the area of T. (We here neglect the ventricular gradient.)

The RS-T Segment When the Initial Deflection is Diphasic.—In Fig. 1*D*, we may imagine that the precordial lead wire is moved to a position which gives an R and an S wave that are precisely equal in area. The R is produced by a wall nearer the electrode; the S is caused by the wave of excitation moving away from the chest lead contact into walls

more remote from the chest surface. The lower, inverted RS-T and T are as in Fig. 1*A*, and correspond to the R of that figure. The upper, upright RS-T and T would follow an equally large S. In this figure, R and S partly combine, so that the area of each is reduced. By summation, the RS-T segment and diphasic T wave shown by the solid line would follow the diphasic initial deflection, R and S. Since the lower curve begins before the upper one, the summated curve will show very slight depression of RS-T. This slight depression may sometimes be large enough to be observed in the human record, as after full or excessive digitalization, with abolition of the gradient.



1D

Fig. 1*D*.—The middle curve shows the form of the RS-T segment and T wave when R and S waves of equal size are present.

The Effect of the Gradient Upon the RS-T Segment.—With the exception of some digitalized hearts, one rarely observes a human heart which does not possess a ventricular gradient. The gradient was defined and experimentally demonstrated by Wilson and his coworkers,[10, 11] and has been studied in the previous papers of this series.[12, 14] Although it was suggested that the presence of the gradient results from different time courses of repolarization of different cardiac surfaces or regions, this is not the only conceivable explanation,[15] although it seems to be the most probable one. In view of our ignorance regarding the cause of the gradient, in Fig. 2, *A*, a quantity representing the gradient is not added by changing the duration of the two monophasic curves, as might be done. Instead, following the R wave, a T wave of approximately normal form and size is arbitrarily drawn in. If we take this ventricular

complex, R and T, to be from one limb lead, then the electrical effect of the gradient, as projected upon the line of the lead, will be equal to the area between the lower RS-T and T curve, and the upper T curve, that is, to area T′ plus area T, as shown. Since the area T′ (the inverted T) equals the area R, then, by substitution, we see that area R plus area T (the upright T) equals the projected area or value of the gradient. Similarly, the area can be measured in another limb lead, and, from the two lead values, the direction and manifest magnitude of the ventricular gradient, as projected on the frontal plane, can be ascertained, as our previous papers explained.[12]

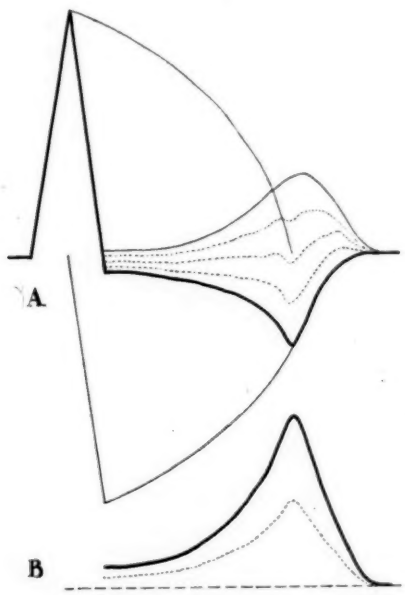


Fig. 2.—*A*, The lower RS-T segment and T wave are those produced when the heart rate is intermediate between the rates of Figs. 1*A* and 1*B*. A T wave of approximately normal form is drawn in arbitrarily. As explained in the text, curve *B* of this figure is the electrical effect of the ventricular gradient as projected on the lead line. It is derived by plotting the vertical distances between the lower and upper RS-T segments and T waves. The dotted lines represent the effect of reducing the magnitude of the "gradient" by (a) 25 per cent; (b) 50 per cent; and (c) 75 per cent. Note how these reductions influence the deviation of the RS-T segment, and how the gradient may "elevate" the segment. The "gradient" corresponding to the middle dotted line in *A* is shown by the dotted line in *B*.

If, at each instant in time, one measures the vertical distance between the profile lines of T′ and T, and plots them as in Fig. 2, *B*, it is evident that the curve of Fig. 2, *B*, shows the temporal development and magnitude of the potential differences from whose sum in two limb leads the ventricular gradient can be found. The curve has the appearance of an isolated, and, in this case, rather high, T wave.

It should be clear from our discussion, so far, that if R and S were negligibly small, and the T wave were relatively very large in a normal human heart, the T wave would give directly the form and magnitude of the ventricular gradient as projected on the line of the lead. But

such electrocardiograms, from normal subjects, are difficult to find, although they may be closely approximated. The form shown in Fig. 2, *B*, is close to that which is observed. Before the QRS complex is completed, the gradient has already begun to develop, and its rise opposes the depression of the RS-T segment. Depending upon conditions, the gradient may overbalance the RS-T depression, so that an actual elevation of the segment appears, as shown in Fig. 2, *A;* it may simply fully offset the depression; or it may fail to compensate for the depression, and some depression appears.

The Effect of Changes in Gradient Magnitude Upon the RS-T Segment.—Also in Fig. 2, *A*, are shown (dotted lines) the effect of reducing the gradient amplitude (a) by 25 per cent; (b) by 50 per cent; and (c) by 75 per cent. The form of the gradient is assumed to be unaffected. The QRS (R) remains essentially unchanged, except to the slight extent that the beginning of the development of the gradient potential difference affects it. It will be seen that the 50 per cent reduction produced a notch in the T wave (middle dotted line in Fig. 2, *A*). Remarkably enough, such a notch is not at all uncommon, especially in the precordial lead, although it is usually not so sharp, probably because of the temporal dispersion of the potential changes in different regions. However, equal gradient reductions may occur without notching, and notching, of course, may possibly occur without reduction in gradient magnitude. It is likely that the time relations between T′ and T differ from heart to heart. This is something which can, at present, be only inferred. It is interesting that in thyrotoxicosis, which will produce a sharper T′ (Fig. 2, *A*), notching of the T wave is not uncommon. In this connection, it should be noted that forms of the T shown in Fig. 2, *A*, should be looked for only in leads which show a fairly large R (or S) wave, with the other wave, S (or R), absent or small. Otherwise the situation is complicated, as Fig. 1*D* shows. It is evident that an analysis of the T wave along these lines necessitates careful examination of thousands of electrocardiograms and a careful consideration of factors which are not relevant to the present paper, together with a more thorough analysis than is here required.

It should be emphasized again that our diagrams are oversimplified, in contrast to the conditions obtaining in the whole human heart. The analysis applies primarily to those leads which possess a QRS complex which is mainly unidirectional, but it may also be applied more generally to the three leads of any electrocardiogram, as shown in the next section.

Evidence From the Human Electrocardiogram.—In a previous paper of this series it was demonstrated that augmentation of the heart rate was associated with a decrease in the magnitude of the ventricular gradient.[13] In the foregoing sections it has been shown that an increased net area of the QRS should be associated with an increased de-

viation of the RS-T segment. It was also shown that, with the net QRS area constant and no gradient present, slowing of the heart should *lessen* the extent of the RS-T segment shift, and vice versa.

In order to test the correctness of these theoretical expectations, twenty-eight electrocardiograms showing some degree of S-T segment "depression" were chosen at random. By "depression" is meant a deviation opposite to the direction of the chief QRS deflection, as in our illustrations. To these twenty-eight records were added, also at random, nine electrocardiograms which revealed no shift, and thirteen with slight "elevation" of the segment, namely, a deviation in the *same* direction as the direction of the chief initial QRS deflection. Various clinical conditions were represented, but care was taken to exclude all records which might show shifts belonging in the second category, as stated in the introduction. Electrocardiograms showing high P waves were excluded because of the frequent difficulty in correcting a segment shift when the end of an auricular T is superposed. The total number of electrocardiograms studied was fifty. Although small, the series proved fully adequate for our purpose, as the reader may judge for himself from Table I.

TABLE I

RS-T SEGMENT DEVIATIONS IN THE ELECTROCARDIOGRAMS OF FIFTY PATIENTS

$G/A_{QRS} < 0.9$				$G/A_{QRS} = 0.9$ to 1.5				$G/A_{QRS} > 1.5$			
A_{QRS} RATE HIGH	LARGE RATE LOW	A_{QRS} RATE HIGH	SMALL RATE LOW	A_{QRS} RATE HIGH	LARGE RATE LOW	A_{QRS} RATE HIGH	SMALL RATE LOW	A_{QRS} RATE HIGH	LARGE RATE LOW	A_{QRS} RATE HIGH	SMALL RATE LOW
−1.00	−1.20	−0.82	−0.45	−1.00	−0.20	−1.00	−0.45	-	+0.80	+0.40	+0.55
−1.00	−0.50	−0.80	0	−0.85	0	−0.55			+0.60	+0.30	+0.42
	−0.45	−0.40		−0.70		−0.45			+0.33	0	+0.40
	−0.33			−0.60		−0.35			0	0	+0.40
	−0.25			−0.35		0				−0.10	+0.30
				−0.30						−0.22	+0.30
				−0.20							+0.10
											0
											0
											0
											0
											−0.10
											−0.33

Note: A minus sign means that the manifest magnitude of the deviation, in *millimeters* (0.1 mV), is opposite to the direction of the chief deflections of the QRS complex. A plus sign means that the deviation is in the same direction.

In the case of each electrocardiogram, the manifest magnitudes of the net QRS areas (A_{QRS}) and of the ventricular gradient (G) were ascertained,[12] and the directions of A_{QRS} and G were also calculated. If any deviation of the RS-T segments was present in the limb leads, the manifest magnitude and approximate direction of the deviation were ascertained. In this connection it should be pointed out that when, as in left ventricular hypertrophy and left axis deviation, RS-T is depressed in Lead I and elevated in Lead III, as is so frequently the case, it is wholly fallacious to summate the deviations in the three leads in order to esti-

mate the magnitude of the deviations. For example, suppose the deviations are respectively minus 1.00 mm. and plus 1.00 mm. in Leads I and III. The direction of the shift is then plus 150 degrees, and the manifest potential of the shift is 1.15 mm.[12] The current practice of adding the magnitudes of the deviations in the three limb leads, without consideration of associated factors or of the true manifest magnitude of the shift, can only lead to confusing and unreliable results. Even though, in practice, the method has been of some value, it could be made more valuable if the problem were approached scientifically.

Since a large net QRS area, other things being equal, produces a large RS-T shift in the absence of a gradient, it is evident that we can not make a simple comparison of that area and the shift. To offset a large RS-T depression after a large R, a proportionately large gradient is required, and, vice versa, a proportionately small gradient will offset the depression after a small R. For this reason, to make the analysis valid, the manifest area of the ventricular gradient, G, was divided by the mean manifest area of QRS or A_{QRS}, in each case. In Table I the fifty electrocardiograms are divided into three groups: in one, the ratio, G/A_{QRS}, is below 0.9; in the second, the ratio is 0.9 to 1.5; in the third, the ratio is over 1.5. (The usual ratio, at ordinary heart rates, averages slightly over 2.0.)

Each of these groups was then subdivided into two, one with an A_{QRS} of 8.0 units (32.0 microvolt-seconds), or above, the other below 8.0 units.[12] The reason for this subdivision can be made clear as follows: When the ratio, G/A_{QRS}, is large, no segment depression is to be expected in either case. But if the ratio were 0, that is, if a gradient were absent, then, as shown in the theoretical discussion, the segment shift will be larger when A_{QRS} is large than when it is small. Similarly, therefore, any decrease in gradient magnitude will produce a proportionately greater depression in the presence of the larger A_{QRS} value. Even though the number of cases is small, the figures in the table fully justify this subdivision, and experience also demonstrates that the largest deviations occur in the presence of large A_{QRS} areas.

A further subdivision separated each subgroup into those in which the heart rate was over 85 and those with rates of 85 or less. This was necessary because, as we have seen, an increased rate produces a greater RS-T depression, and a relatively large gradient is, therefore, needed to offset it.

As inspection of the table demonstrates, the hearts with large A_{QRS} values, rapid rates, and smaller G/A_{QRS} ratios have, on the average, the greatest manifest RS-T depressions; whereas the hearts with smaller A_{QRS} values, slower rates, and larger G/A_{QRS} ratios show fewest RS-T depressions and the greatest number of elevations. In every detail, the results of this study of the human electrocardiogram are in accord with the theoretical explanations we have given.

The larger segment deviations were practically opposite in direction to the mean QRS axis. This is also in accordance with theoretical expectation.

It is purely a matter of chance that the manifest magnitude of the RS-T deviation did not exceed 1.2 mm. in any of our cases chosen at random. In rapid hearts with large QRS areas and small gradients, the shift may often exceed this figure. Even in quite normal hearts, under certain conditions, large deviations may be observed. In Fig. 6 of the second paper in this series,[13] from a normal student while standing, the manifest magnitude of the depression is about 1.5 mm., after allowance for an auricular T wave. The electrocardiogram from the same student, taken in the supine position, shows a clear depression, especially of $RS\text{-}T_3$, which is due to the large R wave area, to a relatively small gradient, and to a rather large angle (as explained below) between the vectors, A_{QRS} and G. Electrocardiograms of this type are not very uncommon. They emphasize the purely physiologic nature of this type of deviation.

The Effect of the Projection of the Gradient Upon the Line of the Lead of the Electrocardiogram.—In the foregoing discussion, it has been tacitly assumed that the directions of the vectors, $\hat{A}_{QRS}$ and $\hat{G}$, are the same. Actually, of course, as the earlier papers demonstrated, this is rarely true, yet in a majority of electrocardiograms the angle between the two axes is not large, and the effect of their divergence can be neglected. The following general statement of the effect of such divergence is probably the best. If the directions of $\hat{A}_{QRS}$ and $\hat{G}$, as projected on the line of any of the three limb leads, are the same, the effect of G will be to oppose the "repolarization" RS-T deviation, and the magnitude of the opposition will be proportional to the magnitude of $\hat{G}$ as it is projected on the lead line. This statement involves the assumption that the time course of development of the electrical forces giving rise to the gradient is similar in different hearts. On the other hand, if the directions of $\hat{A}_{QRS}$ and $\hat{G}$, as projected on the line of any of the leads, are opposite, the effect of the gradient will be to exaggerate the "repolarization deviation" (see discussion below), and the degree of the augmentation will be proportional to the magnitude of the projected $\hat{G}$. Of course, if the direction of the gradient is at right angles to the line of the lead, its magnitude in that lead will be zero, and it will have no effect upon the "repolarization deviation."

Fig. 3, from a syphilitic patient with no clear evidence of heart disease, illustrates this phenomenon. The mean QRS axis is plus 110 degrees and G is at plus 57 degrees. As projected on Lead I, $\hat{A}_{QRS}$ points from the left arm to the right arm, and repolarization following the large S should give an "elevation" of the segment. $\hat{G}$, as projected, points from the right to left arm, and here augments the "elevation" due to repolarization. As projected on Lead II, $\hat{A}_{QRS}$ and $\hat{G}$ are in the same direction, and the effects balance so that no measurable segment

deviation appears. In Lead III, again, the directions are the same, as projected, but G is relatively small in this lead and does not fully offset the "repolarization deviation," and the segment is "depressed." Another example, with left axis deviation in this case, is shown in Fig. 4.

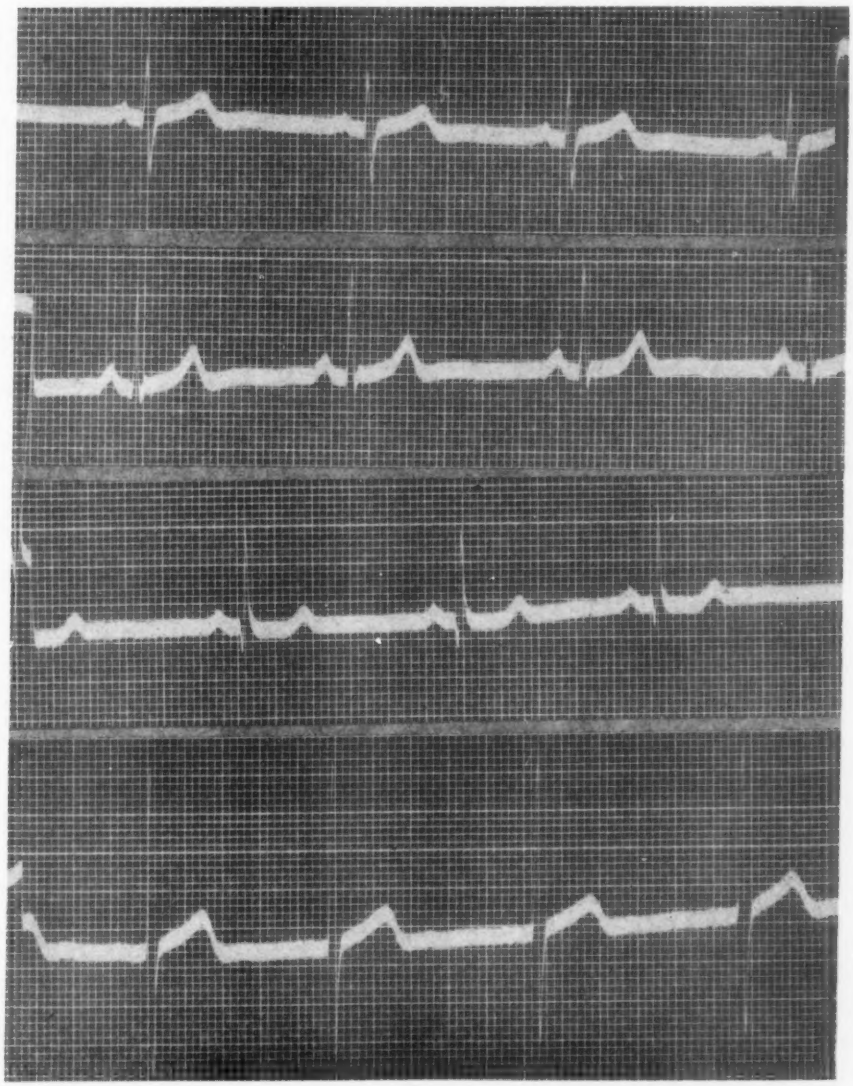


Fig. 3.—Electrocardiogram discussed in text. A colored man, 26 years old. Wassermann positive. Complaints of pain in right hemithorax and shortness of breath in morning. Lower curve, Lead IV F.

The direction of $\hat{A}_{QRS}$ was estimated at minus 27 degrees, and, of $\hat{G}$, at minus 20 degrees, i.e., nearly the same. In this case the two factors are opposed in all leads, as in most electrocardiograms, but the very large gradient produces an elevation of RS-T_1 and a depression of RS-T_3.

Figs. 4 and 6 in the second paper of this series show deviations which are mainly due to a relatively small G/A_{QRS} ratio.

Segment Deviations Due to Other Causes.—As explained in the introduction, segment shifts are of two main types: (a) those associated with reduction in the magnitude of the ventricular gradient, and (b) those due to blocking of excitation waves, either in the presence or absence of a current of injury. The latter type has been explained most recently by Bayley.[1]

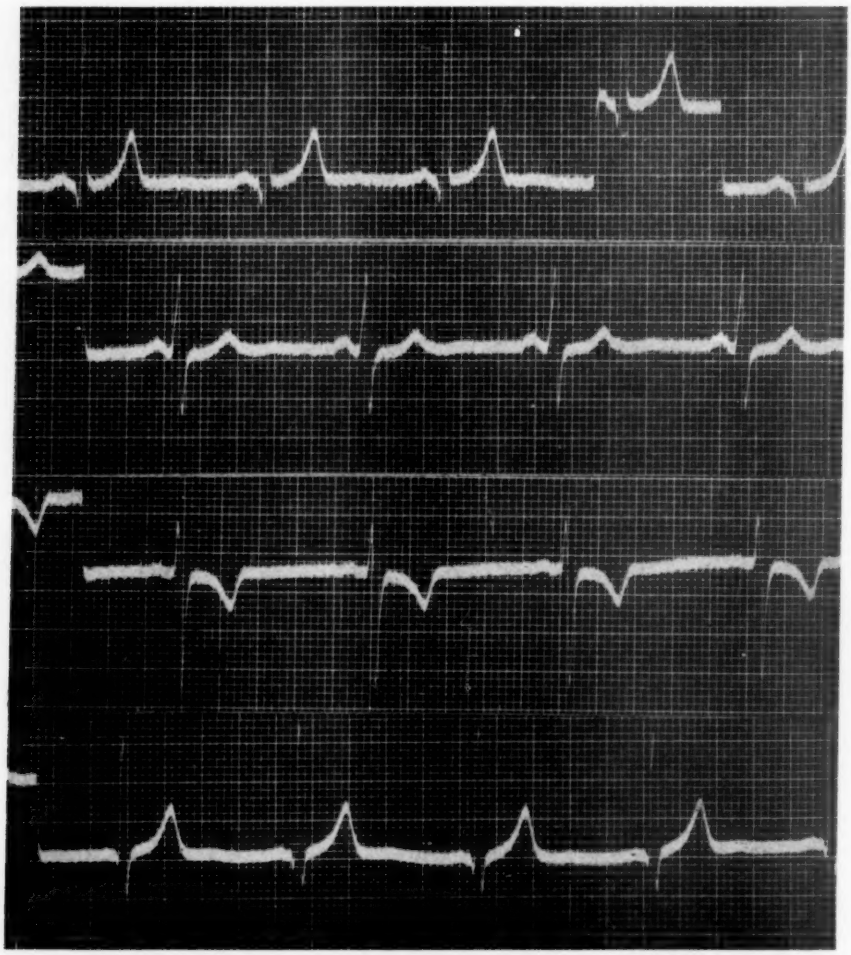


Fig. 4.—Electrocardiogram of a white man, aged 52 years. Admitted to hospital for hernia. No cardiac complaints. Blood pressure reported as 138/100. A_{QRS}, minus 27 degrees; G, minus 20 degrees. Strong counterclockwise rotation of heart on long axis. Since the patient was seated when the electrocardiogram was recorded, it may be within normal limits, although some left ventricular hypertrophy is probable. In 1940, the electrocardiogram was regarded as abnormal. Lower curve, Lead CF_4.

In addition to these two types of RS-T segment shift, it is possible that a third type exists which can be ascribed neither to diminution in the magnitude of the gradient nor to recent muscle damage. In these cases, the direction of the deviation is like that in the physiologic type, but its

extent cannot readily be explained as the result of a simple reduction in gradient magnitude, for G may be normally large. In my experience, curves of this sort are most frequently observed in middle-aged or older women, and are of the type Scherf and Boyd[16] ascribe to "ovarian deficiency." Since there is no heart disease in many cases, the factors responsible must be physiologic. Most probably this group of shifts is merely a variant of the physiologic type, and it can be ascribed to a slow initial development of the potential responsible for the gradient, or, otherwise stated, to a change in the time course of repolarization of the muscle. The two examples of "depressed" segments shown in the column at the extreme right in Table I were from middle-aged women, and one of these is negligibly small. In the present paper, deviations associated with the large, wide T waves ascribed to myocardial ischemia are not considered. They may possibly require special treatment.

Left Ventricular Hypertrophy.—In left ventricular hypertrophy the deviations commonly observed are purely of the physiologic type. They are, therefore, opposite in direction to the chief initial deflection. If there is a high R_1 and a deep S_3, the segment is depressed in Lead I and elevated in Lead III. If, as is not very unusual, there is a fairly high R in all three limb leads, and only small S waves, the segment is commonly depressed in all three leads. These relationships have been studied in a large number of cases, and are reasonably consistent. Usually, in left ventricular hypertrophy of significant degree, the magnitude of the ventricular gradient is normal if there has been no left ventricular failure; after, or certainly during, failure, the magnitude, G, decreases as a rule. In the first condition, segment deviations are due to the increase in the area, A_{QRS}. After failure, both the increased A_{QRS} and the reduced G contribute to augmentation of the shift.

DISCUSSION

In the foregoing paragraphs it has been demonstrated that deviations of the RS-T segment of the type not associated with blocking of impulses within the living myocardium are physiologic, and are merely manifestations of the normal and necessary repolarization of the muscle. After digitalization of a patient, the deviations observed are produced by the same mechanism, although digitalis probably not only reduces the size of the gradient, but also modifies the form of the repolarization curve, as well. In failure of the left ventricle, and in some other conditions which also require careful study, the magnitude of the ventricular gradient is often reduced, and repolarization deviations often appear as a result.

No precise limit can be given for the extent of the deviation, since that varies with the net positive or negative area of the QRS complex, with the degree of reduction in the size of the ventricular gradient, and with the heart rate. Digitalis has an effect much like that of cardiac acceleration. Particularly in the precordial lead in left ventricular hy-

pertrophy, when recorded from a point opposite the right ventricle, the R wave is small and the S wave is often very large. Then either digitalis or an increase in heart rate may produce a deviation upward of the RS-T segment of several millimeters, and the picture sometimes closely resembles that observed ofter infaretion of the anterior left ventricular wall. Similarly, a large R wave in the chest lead may be followed by a depression of the segment like that which occurs with recent infarction of the posterior ventricular wall. This is one reason why the facts herein presented are important.

In using the exercise or anoxia test for coronary insufficiency, an appreciation of the causes of normal deviations is desirable. It is true of the published records (for example, the paper by Twiss and Sokolow[17]) that the changes are undoubtedly significant, and not to be explained by a physiologic change that is likely to occur in the normal heart under the conditions given. But in less expert hands, especially when there is considerable acceleration and when the R or S waves are large, a wholly unspecific change might easily be regarded as significant. This is another reason for stressing the facts of this report. Exercise does not often reverse the direction of a T wave of fair amplitude in the normal person, but the T-wave inversions produced by the standing posture in Fig. 6 of a previous paper[13] are worthy of note.

Another application of the facts of this paper is open to further development. A knowledge of the A_{QRS} area, the gradient magnitude, the Q-T duration (mainly contingent on the heart rate),[18] and the relative directions of $\hat{A}_{QRS}$ and $\hat{G}$, and a knowledge of whether the patient has received digitalis or not, enable one to estimate the approximate magnitude and direction of the expected RS-T segment deviation. If the direction or magnitude of the deviation is not as predicted, or if a deviation is absent when it should be present, then it may become possible to recognize deviations of the second type which may possibly escape recognition by employment of present methods. Obviously, this is a problem which demands much further detailed study.

In conclusion, it may be pointed out again that the names for RS-T segment deviations are unsatisfactory, since they are based upon the superficial appearance of the segment, and take no account of the two entirely different mechanisms of segment production. The names "permanent" and "temporary" have been proposed. But the permanent type, as in left ventricular hypertrophy, is produced by the same mechanism of repolarization as the shifts which appear, for example, on a change from the supine to the standing posture. The shifts due to cardiac acceleration are often more transitory than the deviations due to injury (blocking), which are called "temporary." Better names would seem to be *"repolarization or regression deviations"* for the one type, and *"injury deviations"* for the other. The word injury is used in a broad sense to include any injury or depression of the muscle which is sufficient to block the impulses within the walls. It may be added that in-

traventricular block, as ordinarily defined, does not produce deviations of the injury type, because no intrafiber blocking occurs, or, alternatively, because no current of injury is present.[1] The repolarization deviations are practically always opposite to the larger deflection of QRS, providing the deflection is of fair size and is distinctly larger than the other QRS deflection or deflections. It is, therefore, often superfluous, in such cases, to refer to the direction of the shift as a depression or an elevation. The injury deviations (or shifts) may go in either direction. Hence it seems necessary to indicate the direction, and the terms "depression" or "elevation" are satisfactory.

In addition to the names suggested above, a name also seems needed to describe the deviations, such as those shown in Fig. 4, which are due to the presence of a ventricular gradient. However probable, it is not certain that these are a consequence of repolarization. They might be called "gradient deviations."

Certain other aspects of this problem will be considered in a paper on the T wave, which is now in preparation.

SUMMARY

The analysis of any diphasic ventricular complex of the electrocardiogram from the standpoint that it is produced by the summation of two monophasic curves has certain advantages.

By use of this method it is shown that, other things being equal, the extent of deviation of the RS-T segment, in the absence of a ventricular gradient, or of injury effects, is determined by at least two factors:

1. The net area of the QRS complex.
2. The heart rate or, otherwise stated, the duration of the Q-T interval.

The effect of a diphasic form of the initial ventricular complex is considered.

The effect upon the RS-T segment of the presence of the electrical forces which give rise to the ventricular gradient is discussed from the standpoint (a) of the magnitude of the gradient in relation to the magnitude of the net QRS area; and (b) of the magnitude of the gradient as projected on a lead line in relation to the net QRS area in that lead.

It is shown that the RS-T segment deviations observed in human electrocardiograms agree with the theoretical expectations.

It is suggested that RS-T segment deviations of the type described be called "repolarization or regression deviations"; that those produced by injury or muscle depression and blocking be called "injury deviations"; and that the characteristic slight deviations due to the presence of a large ventricular gradient be called "gradient deviations." If it should be found that other mechanisms of segment deviations exist, other categories may be included.

A few clinical applications of these observations are briefly stated.

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ANOMALOUS ORIGINS OF THE POSTERIOR INTERCOSTAL ARTERIES FROM 915 THORACIC AORTAS: THEIR ROLE IN FRACTURES OF THE RIBS

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A NUMBER of years ago, after World War I, the discovery of fractured ribs at post-mortem examination of patients in Massachusetts hospitals for mental diseases led to inquiries of how they were received and whether external force was applied, and, if so, in what manner. These fractures occurred in men almost entirely, were frequently bilateral, and involved the fourth to eighth ribs. The circumstances led to the conclusion that they were traumatic in origin. A staunch clinician held that they were done post mortem, but, in view of the fact that they were attended by free hemorrhage in surrounding tissues, that claim was not substantiated. No thought had at that time been given to the possibility of change in the ribs caused by a reduced circulation, either by anomaly of their arteries, or sclerosis of the aorta narrowing or occluding the origins of the intercostal arteries.

It had been found in 1917, when mental hospitals were short of help because of military enlistments, that the amount of pulling force required to fracture a rib could be ascertained by means of a brass arm and scale devised by a professor at the Massachusetts Institute of Technology. This arm was hooked on to the median tip of ribs isolated by removing their bordering muscles after the sternum was cut away, and the instrument manually lifted. The figures registered on the scale varied from ½ pound to 18 pounds. In sixteen instances, the ribs were tested by the device mentioned. Eleven of the patients were men and five were women. Their ages were from 24 to 79 years. There were no normal controls because the autopsies were done on those suffering from mental disease or defect. After a time the test was given up because of the press of other inquiries.

The increase in the amount of *pulling* force required in most cases to cause a fracture, as one progresses from the upper ribs to the lower, may have some significance. It takes more force to break a bony circle than an ellipse, which the upper four ribs resemble; moreover, it is more awkward to apply force externally high on the chest than lower, even if it takes more force to fracture the lower ribs. This, together with the greater protection of the upper chest by the arms, may explain why more fractures occur in the lower ribs. Falls against tables, bed frames, chairs, or toilet bowls could hardly reach above the nipple line. Bilateral crushing pressure, applied from behind the patient, or a knee

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on a chest, can be effective in a short time, but again such fractures tend to occur in the lower group of ribs.

In the sixteen instances mentioned, the five women were over 70 years old, and it took only ½ pound to 5 pounds to break the ribs from above downward. Five of the men were under 50 years of age, and it took from 2 to 18 pounds to cause a fracture; in the six who were over 50 years of age, ½ pound to 10 pounds were required. In this group the condition of the aorta or the presence of debilitating diseases is too small to be considered.

Campbell[1] used a simple instrument with a stirrup and screw, the turning of which against a convexity and concavity of the eighth rib post mortem would register the breaking strain. The first fact he was able to discern was that it would require 66 pounds of pressure to break the toughest rib, and this amount would lessen, with increase in age and the presence of debilitating diseases. He stated that ribs of women would break at half the strain required for men. He gives a condensed table in his second report,[2] which is shown in Table I.

TABLE I

	MALES		FEMALES	
	AGAINST THE CONVEXITY	AGAINST THE CONCAVITY	AGAINST THE CONVEXITY	AGAINST THE CONCAVITY
58 Insane	41.04 lb.	42.14 lb.	20.68 lb.	20.90 lb.
58 Sane	42.73 lb.	42.63 lb.	23 lb.	23.3 lb.

This compares the breaking strain of the eighth rib in both sexes of various ages in a series of 58 sane and 58 insane persons. It was Campbell's idea that it was not mental diseases, but the debilities that accompanied them, that made the ribs somewhat more vulnerable, as, for example, tuberculosis and syphilis. He, of course, mentions self-injury in excited periods and rough methods of handling.

Whether "strain" (Campbell), or "pulling force" (Canavan), registered by mechanical means on the dead rib, has any bearing on the amount of trauma presented to the living has apparently not yet been recorded. A simpler way would be to apply the finger and thumb force to the isolated rib.

For years the discovery at autopsy of broken ribs was charged up to the disciplinary methods of the men who were then procurable as attendants.

Dr. Leary's[3] observations on the effects of alcohol on the human body surprised many workers when he announced that alcohol, when taken in sufficient quantities to brand a person as an alcoholic, was not responsible for sclerosing the aorta. In other words, an advanced alcoholic had a smooth aorta. Dr. Leary's observations regarding the effect of alcohol on aortas were made in his active service as medical examiner, where he could catch his patients red-handed as to habits. Our aortas were from patients with varying length of residence in mental or gen-

eral hospitals, where time and other factors might disguise the lack of alcoholic effects on the aortas. His observations, however, were a signal to examine carefully all aortas post mortem, and thus the anomalous intercostal branches from the thoracic aorta came to light.

From my own service and from numerous friends engaged in pathologic work in Massachusetts and other states, aortas were received fixed in formalin. It would have been advantageous had all these vessels been flattened against the inner wall of a good-sized round glass jar containing a 10 per cent solution of formalin, thus preventing distortion. However, the good will of the donors offset these difficulties, for they not only saved and sent the specimens, but furnished clinical data, such as hospital and autopsy number for identification, the age and sex of the patient, history or no history of alcoholism, and the presence or absence of syphilis. Particularly am I indebted to Dr. William Freeman, Dr. B. E. Clarke, Dr. Donald J. Henderson, and Dr. I. B. Akerson. A total of 915 unselected aortas were collected.

There were 473 males and 371 females. In the remaining 71 cases the sex was not recorded. Their ages, arranged by decades, are given in Table II.

TABLE II

AGES IN DECADES	NUMBER OF CASES
0-10	17
11-20	11
21-30	33
31-40	78
41-50	96
51-60	143
61-70	191
71-80	191
81-90	68
91-100	5
101-110	1
Unknown	81

Most of the aortas came from those who had attained ages from 31 to 90 years, but there were some from younger persons, even premature babies.

Since no bone or portion thereof could be used as a landmark for the removed aorta, one of the main upper branches of the arch, the subclavian artery, was considered the upper limit, and the diaphragm the lower limit, of the thoracic aorta. The usual procedure, at autopsy, to reveal disease of the aorta is to make a ventral cut from the bifurcation of the aorta to its arch, in situ; in fact, any other approach would be awkward. This leaves the renal arteries, if normal, in a bilateral position as guides to the posterior midline of the aorta, where the paired segmental origin of the posterior intercostal arteries of the thoracic aorta should arise.

Adachi,[4] in his painstaking work on the human arterial system of 196 Japanese subjects, pointed out that in the fifteen thoracic aortas which he studied there was a deviation to the right or left of the posterior

median line for the origin of the posterior intercostal arteries from the thoracic aorta. It was indicated that these deviations were caused by the rotation of the developing esophagus and aorta in the embryonic period.

Fig. 1. Fig. 2.

Fig. 1.—Group I. Paired intercostal arteries arising in the posterior midline of the aorta.

Fig. 2.—Group I. Same, showing the effect of arteriosclerosis of the aorta on the origins of the intercostal arteries.

This proved to be, for the most part, an excellent way to sort out the types of origins of these same branches from the 915 aortas in the present series. Taking the expected posterior mid-locations of the nine pairs of intercostal arteries first, they were found so placed in 231 instances (25.2 per cent). Of course, there were the inevitable "variations" from this criterion, but if more than half of the branches were so placed in a given aorta, they were classified under Group I (Figs. 1 and 2), even though some might appear as a single large or a single small opening in some localities, or present themselves focally in triads.

With the same leeway, Group II (Fig. 3) contains those which, nearest the subclavian, were found on the left of the median line, but deviated to the right of it before the level of the diaphragm was reached.

Fig. 3. Fig. 4.

Fig. 3.—Group II. Note that upper orifices of the intercostals hold to the left of the central lines; lower pairs to the right.

Fig. 4.—Group III. Here is the reverse of Group II. The upper pairs are on the right; lower ones make their way to the left.

This occurred in 41, or 4.5 per cent, of the cases. Those in Group III (Fig. 4) were in reverse of the latter, i.e., were on the right side nearest the subclavian and migrated toward the left as they descended; this group included 71 cases (7.8 per cent). Those in Group IV (Fig. 5) were much more definitely on the right all the way, and this occurred in 314 instances (34.3 per cent). Those making up Group V (Fig. 6) were all on the left of the median line; of these there were 168 cases (18.4 per cent), or, roughly, half the number which were in totally right-sided placement. The surprise was in Group VI (Fig. 7), which is composed of those showing *anterior* origins of the intercostal arteries,

for this occurred in 75 cases (8.2 per cent). Group VII (Fig. 8) includes those which showed such scattered or miscellaneous origins that they could not be assigned to any of the other groups, elastic as were the criteria for them all. There were 16 such cases (1.7 per cent). Table III presents the origins of the intercostal branchings in the whole series, briefly, in tabular form.

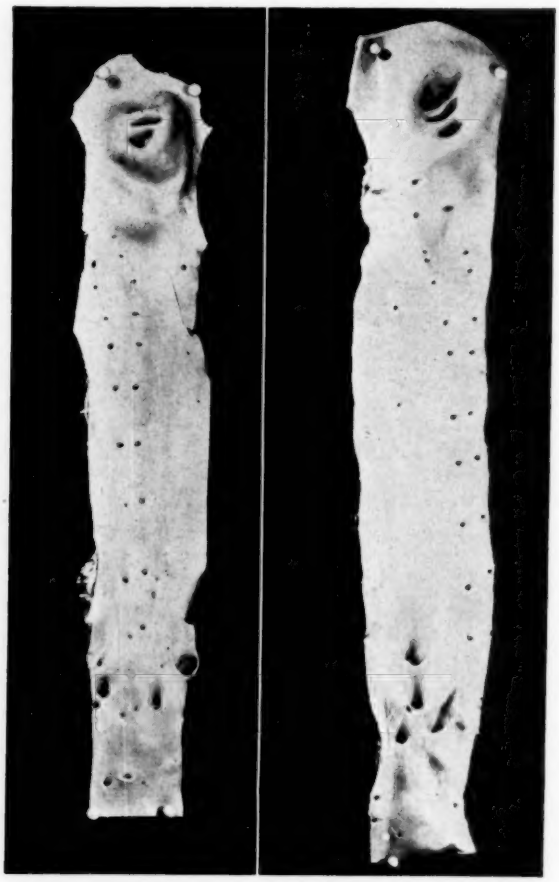

Fig. 5. Fig. 6.

Fig. 5.—Group IV. The paired intercostal arteries are all on the right of the median line.

Fig. 6.—Group V. Here the paired intercostal arteries are all on the left of the median line.

In 673, or 73.6 per cent, of the aortas, these origins were complicated by atherosclerosis or arteriosclerosis, which narrowed or covered the mouths of the thoracic intercostal arteries.

Alcoholism was known to have been included in the history of 92 of the 915 patients whose aortas were studied; of these 92 the aortas were smooth in but 20 (21.7 per cent). Dr. Leary had said, in a conversa-

TABLE III

PAIRED INTERCOSTAL BRANCHINGS FROM THE THORACIC AORTA IN 915 SUBJECTS

GROUP I	GROUP II	GROUP III	GROUP IV	GROUP V	GROUP VI	GROUP VII
Paired in posterior mid-aortic line. 231, or 25.2 %	Upper on left; lower on right. 41, or 4.5 %	Upper on right; lower on left. 71, or 7.8 %	All on right. 314, or 34.3 %	All on left. 168, or 18.4 %	All anterior. 75, or 8.2 %	Scattered and miscellaneous. 16, or 1.7 %

Fig. 7.

Fig. 8.

Fig. 7.—Group VI. This demonstrates complete half swing of intercostal arteries to the anterior wall of the aorta.

Fig. 8.—Group VII. The scattering of origin of intercostal arteries is complicated by advanced sclerosis of the aorta.

tion, that, for the best effect, that is, from the standpoint of smoothness of aortas, the patients would have to be "drunk every day," which he considered "expensive."

Among the 915 aortas, 84 (9.2 per cent) had belonged to patients who were known to have had syphilis, and in 14 of the 84 (16.7 per cent) a tertiary lesion in the aorta was recognized.

From a surgical standpoint the muscular branches of the intercostals are of most interest, for accidental wounds or even carefully planned thoracic surgical procedures may open anomalous branches, with resultant hematomas of various sizes. In the literature, early reports concerning intercostal arteries dealt mainly with hemorrhages from wounds or rupture of these vessels from vertebral caries.

COMMENT

If the ribs, which are among the main sources of erythrocytes,[5] may be considered to receive their blood supply from the anterior and posterior intercostal arteries, although no textbook which I consulted states this as a fact, the majority of them in this group of 915 cases had handicaps. These handicaps consisted of anomalies of origin of the posterior intercostal arteries in 685 (74.9 per cent) of the aortas, and sclerosis of the aorta contributing to diminished blood supply because of diminishing the size, or sometimes occluding their orifices, in 673 (73.6 per cent). This may be the answer to our original quest for a reason for the perplexing incidence of fractured ribs at post-mortem examination of these patients. They may have had anomalous, or closed, intercostal artery origins.

SUMMARY

Nine hundred fifteen aortas were collected from various hospitals during the years 1934 to 1937. All had been fixed in a 10 per cent solution of formalin, and all but three were believed to have been opened anteriorly. The subclavian artery was considered the upper limit of the thoracic aorta, and the diaphragm, the lower.

Nine pairs of intercostal arteries should arise in the posterior midline of the aorta above the diaphragm. With allowances for variations, this was found to be true in 25.2 per cent of the cases.

In 74.8 per cent they deviated to the right, to the left, or to the anterior wall, or were scattered in their placement of origin, constituting a devious delivery of blood.

In the 915 aortas, 673, or 73.6 per cent, had thickening or destruction of the aortic intima, further interfering with the nutritional function of the branches.

In 84 patients there had been syphilis, and a tertiary lesion was recognized in fourteen, or 16.7 per cent, of the 84 aortas.

Alcoholism was known to have been included in the history of 92 of the patients, and in these the aortas were smooth in twenty, or 21.7 per cent.

I am greatly indebted to Dr. L. Eisenhardt and Dr. H. L. Weatherford for assistance in the preparation of this paper.

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ATRIAL SEPTAL DEFECT

A Report of Two Cases in Which There Was Recurrent Laryngeal Nerve Paralysis

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AN ATRIAL septal defect, occurring either alone or in association with other developmental or acquired defects of the heart, was present in about 8 per cent of the 1,000 cases of congenital heart disease collected by Abbott.[1] It is not the purpose of this paper to review the already extensive literature on this subject, for an excellent summary of previous reports appeared in connection with an analysis of fifty-two additional cases, by Bedford, Papp, and Parkinson.[2]

The occurrence of an unusual, and apparently rare, complication of this congenital abnormality, together with the fact that patency of the ductus arteriosus was incorrectly diagnosed in one instance and a substernal goiter was suspected in the other, makes the following two cases worthy of a fairly detailed report.

Case 1.—B. F. M. (Med. No. 60102), 23 years old, white, single, a graduate of a teacher's college, was referred to one of us (S. A. L.) on July 24, 1941, with a diagnosis of patency of the ductus arteriosus, to be studied preparatory to ligation of the congenitally patent vessel.

Her chief complaint was partial loss of voice of three and one-half months' duration.

The family history was not contributory. The past history was not significant, except as will be noted in relation to the present illness.

Present Illness.—She stated that she was a blue baby at birth, but did not know how long this had persisted. Five years before entry, a physician had informed her that she had a cardiac murmur, but, to the patient's knowledge, no definite diagnosis was made. She had enjoyed good health except that physical activity had been moderately restricted because of fatigability and moderate dyspnea brought on by exertion. On occasions in the past, after a day of unusual activity, such as engaging in girls' sports, she had found that one week of rest was required to regain her usual feeling of well-being. There has been no further cyanosis as far as she knew, except that, when in swimming, there was some blueness about the nose and mouth. However, in spite of the dyspnea, she had been able to carry the full course of a student school teacher, including minor school gymnastics.

Three and one-half months before entry, in order to be on time for an interview for a position as school teacher, she ran one block and then ran up two flights of stairs. Immediately after this exertion, she found, to her utter embarrassment, that she was unable to speak. This was not complete aphonia, but inability to speak audibly. During the next two months her voice slowly returned, but had not yet regained its normal

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quality. This was most noticeable to the patient on raising her voice to speak to persons at a distance; the voice at these times lost its normal resonance and inflection, and occasionally became very gruff. Two weeks before entry she had consulted her private physician because of the impairment of her voice and decreased exercise tolerance. A diagnosis of patency of the ductus arteriosus was made, and the patient was referred to us for study preparatory to surgical obliteration of the abnormal vessel.

Pain of cardiac origin, orthopnea, and dependent edema had never been present. There was no history of rheumatic fever, growing pains, chorea, or frequent sore throats.

Physical Examination.—The patient was well developed and well nourished. She was able to lie flat in bed without any discomfort whatsoever. There was no cyanosis or clubbing of the fingers or toes. The voice seemed to be normal, but the patient stated that it did not have its usual quality. The head and neck were normal. The thyroid gland, although palpable, was not enlarged. There were no abnormal pulsations or thrills in the cervical vessels. The chest was negative to percussion and auscultation. The heart was slightly enlarged. The rhythm was normal, and the rate was 96. A prominent systolic pulsation was both visible and palpable on the anterior superior aspect of the left side of the chest, most marked in the second intercostal space immediately to the left of the sternal border, and a palpable shock corresponding to the pulmonic second sound was noted in the same location. The apical impulse was normal. There was a very soft (Grade I) apical systolic murmur, but no diastolic murmur was audible in this area. As the pulmonic area was approached, both heart sounds became markedly accentuated, especially the second sound. The abnormally loud sounds at the base suggested the presence of a systolic murmur, but the only murmur definitely audible in this area was a soft, early, blowing diastolic murmur, best heard in the second left intercostal space, but also heard to a less degree all along the left sternal border. The blood pressure readings were: right arm, 128/86; left arm, 100/78; left leg, 158/110; right leg, 170/104. After exercise, the blood pressure (right arm) rose to 186/90, with a corresponding rise in the pulse rate. During and after the exertion, she was moderately breathless, but there was no cyanosis or hoarseness.

Laboratory Data.—The blood Hinton and Wassermann reactions were negative. The urine was normal. Examination of the blood revealed a hemoglobin of 110 per cent (Sahli), an erythrocyte count of 5,700,000, a leucocyte count of 6,800, and a normal differential leucocyte count. The blood nonprotein nitrogen was 29 mg. per cent, and the cholesterol, 220 mg. per cent. The vital capacity was 3,200 c.c. The circulation time (decholin method) was 13 seconds, and the venous pressure, 120 mm. saline (right arm).

An electrocardiogram (Fig. 1) showed moderate right axis deviation and inverted T waves in Lead IV, but no other changes.

Fluoroscopic examination and roentgenograms of the heart (Fig. 2) showed definite cardiac enlargement, chiefly downward and to the left, with marked prominence of the pulmonary conus and marked dilatation of the intrapulmonary arteries. The right pulmonary artery measured 3 cm. in diameter, and showed marked systolic expansion. The aorta was indistinct and probably small, but was possibly obscured by the dilated pulmonary artery. There was only slight dilatation of the left

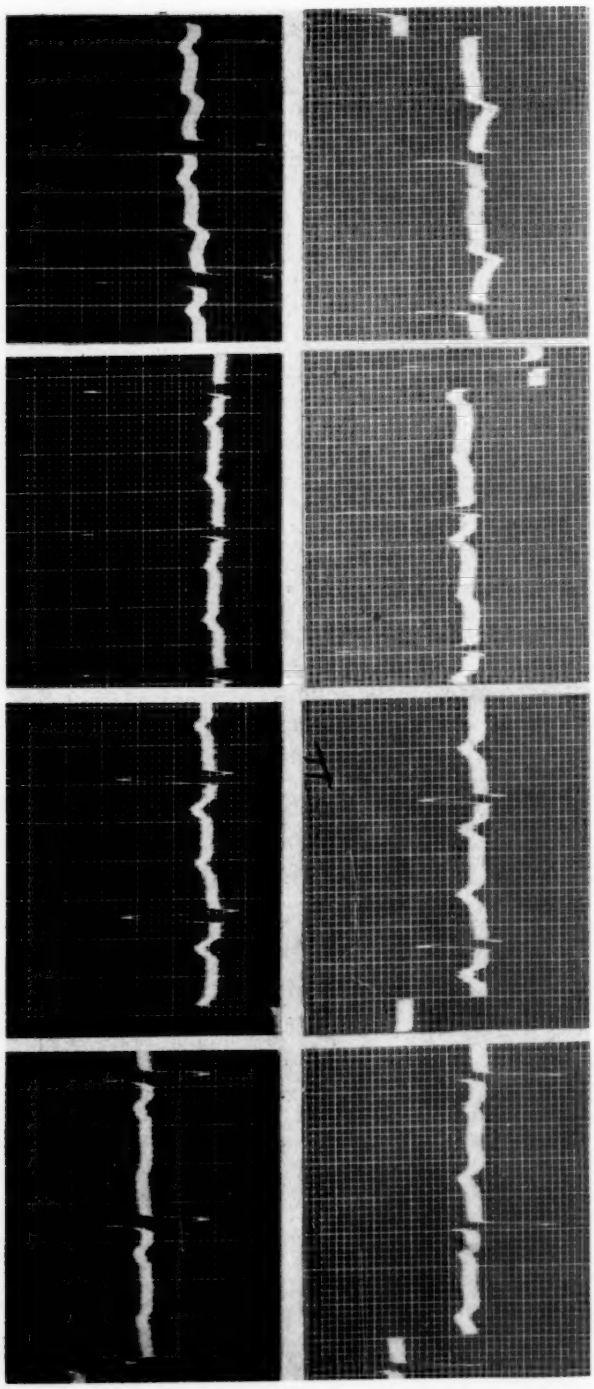

Fig. 1.—The upper tracings are from Case 1; they show well-marked right axis deviation, with normal form of the ventricular complexes, except that T_4 is inverted. The lower tracings, from Case 2, show well-marked right axis deviation, with normal form of the ventricular complex except that T_4 is inverted.

auricle posteriorly. The lungs, other than as mentioned above, were negative. No intracardiac calcification was seen. The measurements were as follows: Mr. 3.2, Ml. 10.8, G.V. 5.0, Int. Diam. 26.8.*

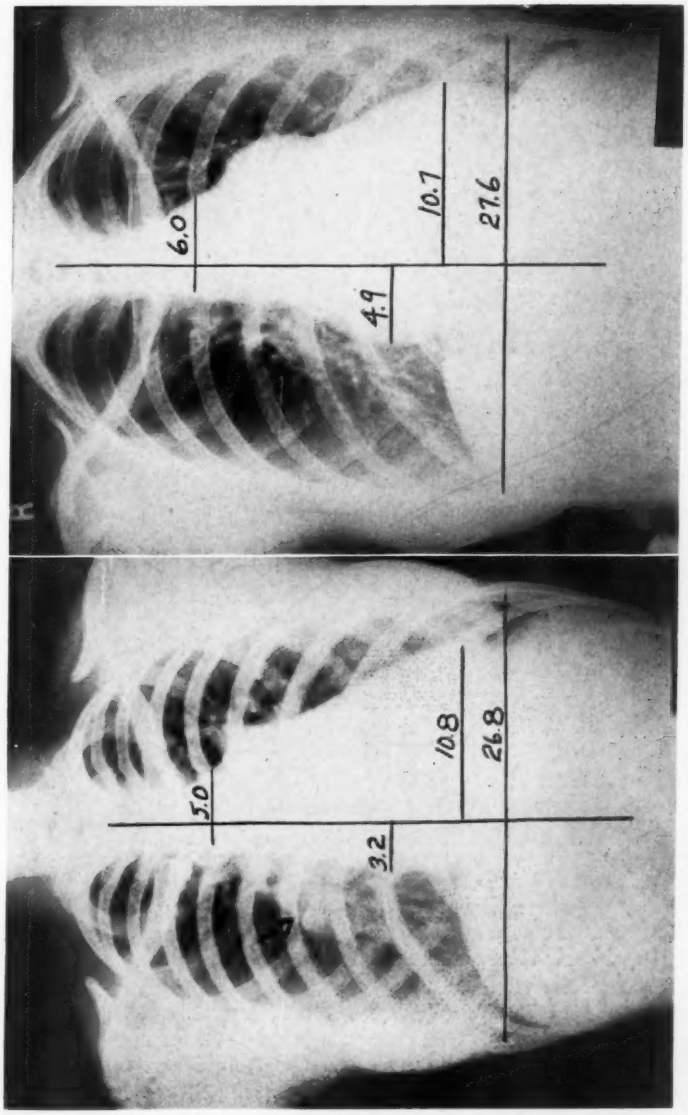

Fig. 2.—Roentgenograph on the left (Case 1) shows slight cardiac enlargement, a very prominent main pulmonary artery, and marked dilatation of the right pulmonary branch (arrow). Roentgenogram on the right (Case 2) shows some general cardiac enlargement, a very prominent main pulmonary artery, and moderate enlargement of the pulmonary branches in the right hilum.

On laryngoscopic examination (by Dr. John R. Richardson) during rest, the left vocal cord was found to lie in the cadaveric position (Fig. 3). On phonation (Fig. 3), the right cord moved across the midline, but did not closely approximate the completely paralyzed left cord; this accounted for the abnormal quality of the voice. Furthermore, the left arytenoid cartilage showed no evidence of movement on phonation. It was the opinion of the examiner that, as time passed, the right cord would move sufficiently well to compensate for the lack of movement of

the left, thereby resulting in an almost complete return of the normal quality of the voice.

Case 2.—L. G. A. (Surg. No. 69113), 40 years old, single, white, a school teacher, was referred to Dr. F. C. Newton, of the surgical staff, on Oct. 7, 1941, for study because of the possibility of a mediastinal goiter.

Although the patient had many complaints, only those referable to the cardiovascular system concern us here. The family history was not contributory. The relevant past history is given with the present illness.

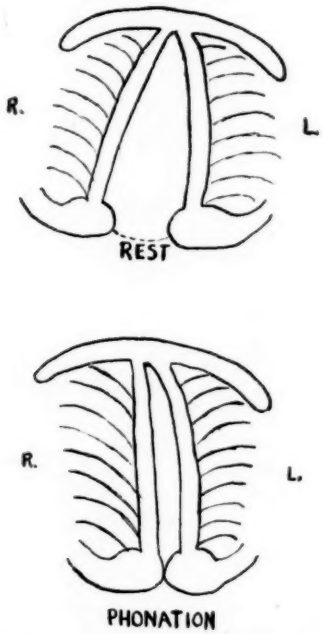

Fig. 3.—Drawing of the appearance of the vocal cords at rest (upper), and with phonation (lower). In both cases the appearance was essentially the same. Note immobility of the left vocal cord and compensatory movement of the right beyond the midline on phonation.

Present Illness.—She stated that she was a blue baby at birth, but did not know how long this had persisted. There was no history of rheumatic fever, growing pains, chorea, or frequent sore throats. Low-grade hoarseness, associated with a hissing sound on normal respiration, had been present since birth. Eleven years before entry, a laryngoscopic examination had been performed in connection with an operation on the nasal septum. She was told that the left vocal cord was paralyzed, and probably had been all her life. The hoarseness had never produced any disability, although it was more pronounced during fatigue and during upper respiratory infections.

Since childhood she had noticed that she was unable to exercise as much as other people because of fatigability and dyspnea. Climbing two flights of stairs produced temporarily incapacitating dyspnea. Mild palpitation had been present constantly, and became more severe on exertion or when she was fatigued. There was no history of cyanosis since birth. Neither orthopnea nor edema of the ankles had ever been present. There had been no pain of cardiac origin.

Physical Examination.—The patient was well developed, slightly obese, and did not appear ill. The temperature and pulse rate were normal. There was very slight cyanosis of the lips and fingernail beds. There was no clubbing of the fingers and toes. There was a small perforation of the nasal septum as a result of her previous operation. The remainder of the head and neck was normal. The thyroid gland was palpable, but was not enlarged or nodular. There were no abnormal pulsations of the cervical vessels. The lungs were normal to percussion and auscultation.

Percussion of the heart showed that the right border of dullness was parasternal, and that the left border of dullness was 7 cm. from the midsternal line (midclavicular line, 7.5 cm.). The rhythm was normal. The pulmonic second sound was markedly accentuated, and there was a long, low-pitched, blowing, diastolic murmur along the left sternal border, most marked in the second left intercostal space. No other murmurs were audible. The blood pressure was 140/90. The remainder of the physical examination was not contributory.

Laboratory Data.—The blood Hinton and Wassermann reactions were negative. The hemoglobin was 100 per cent (Sahli), the erythrocytes numbered 5,500,000, the leucocyte count was 7,600, and the differential leucocyte count was normal. The blood cholesterol was 206 mg. per cent. The vital capacity was 2,900 c.c. An electrocardiogram (Fig. 1) showed right axis deviation and inverted T waves in the fourth lead.

Fluoroscopic examination and posteroanterior and oblique roentgenograms of the heart (Fig. 2) showed definite cardiac enlargement, chiefly of the left ventricle. There was marked prominence of the pulmonary artery, which projected well beyond the heart border just below the arch of the aorta. This area showed expansion with systole which was more marked than normal. The intrapulmonary branches were slightly enlarged on the right, but showed no expansile pulsation. The lungs elsewhere were normal. There was no demonstrable dilatation of the left auricle, nor any intracardiac calcification. The measurements were as follows: Mr. 4.9, MI. 10.7, G.V. 6.0, Int. Diam. 27.6

On laryngoscopic examination (by Dr. Lyman G. Richardson), the vocal cords during the resting state were found to be in the same position as those of the first patient (Fig. 3). However, on phonation, in contrast to the first case, the right cord moved far enough across the midline to compensate for the lack of movement of the paralyzed left cord, thereby resulting in a relatively normal quality of the voice.

COMMENT

The fact that both patients were following the same profession and that both were seen within four months of each other is a peculiar coincidence. Probably the most important clinical feature, however, is that both patients were referred to the hospital with the possibility in mind of surgical intervention, one for patency of the ductus arteriosus and the other for a substernal goiter. Now that surgical obliteration of a patent ductus arteriosus is possible, it is extremely important that every effort be made to arrive at the correct diagnosis in cases of congenital heart disease. This will avoid useless operation, which carries a mortality of 5 to 10 per cent.

The most unusual feature of these two cases was complete paralysis of the left vocal cord, apparently because of functional interruption of the recurrent laryngeal nerve where it loops around the aorta on its course to the neck. Hoarseness is a common complication of aneurysms of the arch of the aorta, and, as might be suspected, it also occurs with aneurysms of the pulmonary artery, the great majority of which are also caused by syphilis.[3-5]

Wahl and Gard[5] presented one case of recurrent laryngeal nerve palsy produced by an aneurysm of the pulmonary artery in a patient with uncomplicated atrial septal defect. A similar case, but with dilatation rather than aneurysm of the pulmonary artery, was reported by Hotz (Case 2).[6] E. Weiss' patient with Lutembacher's syndrome complicated by hoarseness was reported by Abbott.[7] In Bedford, Papp, and Parkinson's Case 3[2] there was transient hoarseness after exertion. That hoarseness does not occur more frequently in congenital heart disease with left-right shunts, which may more than triple pulmonary flow, is rather surprising when one considers the anatomic relationship between the arch of the aorta, the pulmonary artery, and the recurrent laryngeal nerve. As a matter of fact, cases of Eisenmenger's syndrome complicated by recurrent nerve palsy have been reported by Baumgartner and Abbott[8] and by Talley and Fowler.[9] Furthermore, it is to be expected that any congenital cardiac defect that is associated with marked enlargement of the pulmonary artery may be complicated by left vocal cord paralysis.

Fetterolf and Norris,[10] by their careful anatomic dissections, showed that hoarseness in cases of mitral stenosis is caused by compression of the recurrent laryngeal nerve between the dilated pulmonary artery (or the left pulmonary artery) and the inferior surface of the arch of the aorta where the nerve loops around the latter vessel on its way to the neck. From their description, it seems clear that hoarseness may be produced by this mechanism, regardless of the cause of the dilatation of the pulmonary artery. From the history, physical examination, and roentgenologic changes in the cases presented here, one is led to the conclusion that the recurrent nerve paralysis was produced by compression of the nerve between the aorta and the dilated pulmonary artery or one of its branches.

SUMMARY

Two cases of atrial septal defect with the unusual complication of recurrent laryngeal nerve paralysis are presented. The necessity of exact diagnosis of congenital heart disease is stressed because both patients were erroneously suspected of having diseases which are amenable to surgical treatment, namely, patency of the ductus arteriosus in one instance, and substernal goiter in the other.

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THE BASAL METABOLIC RATE IN ESSENTIAL HYPERTENSION

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THE literature relative to the effect of high blood pressure on basal metabolism is confusing because in some instances the authors failed to state the nature of the cases studied, and because, in other instances, patients had complications, such as myocardial failure of varying degrees, Cheyne-Stokes respiration, nephritis, ovarian failure, or possibly hyperthyroidism.[1-6] However, there is evidence that hypertension can increase the basal metabolic rate, but does not always do so.[7-15]

Of these reports, those of Keith and associates,[13] Hayasaka,[11] Weiss,[14] Weiss and Ellis,[15] Becker,[7] Boothby and Sandiford,[8] and Crile and McCullagh[9] are most pertinent to our presentation, which deals with the effect of uncomplicated high blood pressure on the basal metabolic rate. Keith and associates measured the basal metabolic rate in thirty-nine cases of malignant (Group 4) hypertension; in eight instances the basal rate was greater than plus 20 per cent.[13] Although these authors could not explain their observations, they expressed the belief that the thyroid gland was not responsible. Hayasaka obtained an average basal metabolic rate of minus 6 per cent in a group of cases of "benign" hypertension, and an average of plus 18 per cent in a group of "malignant" hypertension. He found that neither the pulse rate nor the diastolic blood pressure was directly related to the basal metabolism. Weiss and Ellis obtained basal metabolic rates varying from plus 15 to plus 50 per cent in seven of eleven patients who had hypertension with normal cardiac function.[15] Although they admitted that the cause for this elevation of the basal rate was unknown, they expressed the belief that an active sympathetic nervous system must be present. One patient of these authors had a basal metabolic rate of plus 45 per cent, associated with a blood pressure of 270/140. Thyroidectomy caused reduction of the rate to normal, but did not influence the blood pressure. In a study of sixteen patients who had essential hypertension and no cardiac failure, Becker noted basal rates varying from plus 17 to plus 38 per cent. He concluded that this phenomenon was due to a thyrogenic component, as he obtained a return of the basal metabolic rate to normal after roentgen treatment of the thyroid gland. The blood pressure decreased in some cases.

On the other hand, Boothby and Sandiford,[8] in a statistical study of 170 patients who had high blood pressure, found that approximately 90 per cent of them had basal metabolic rates within the range of plus 15

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to minus 15 per cent. Crile and McCullagh[9] discussed means of distinguishing an elevated basal metabolic rate in the presence of hypertension from that due to hyperthyroidism. They suggested that the increased basal rate in many cases of hypertension might be the result of the increased cardiovascular activity required to maintain the circulation against a high diastolic blood pressure. Mosler and Edelstein[16] found a normal metabolic rate in "pure" forms of essential hypertension. Kusakabe and Ito[17] found a normal rate in five cases of essential hypertension. The literature is, therefore, conflicting with respect to the basal metabolic rate in uncomplicated essential hypertension. The opinions range from observations that there is almost uniform elevation of the basal metabolic rate to those which indicate that the rate is normal in hypertension. Additional studies relative to the basal metabolism in hypertension may be found in articles by Boas and Shapiro,[18, 19] Fishberg,[10] Hamilton and Knight,[20] Mannaberg,[21] and Rose.[22]

Our method of approach to this problem was a study of case records from the files of the Mayo Clinic. Only records of patients who had essential hypertension and whose basal metabolic rates had been measured were used. From this group were discarded: (1) all cases in which clinically there was even questionable cardiac decompensation;* (2) all cases in which there was definite or probable hyperthyroidism, in the judgment of the consultant who examined the patient; and (3) all cases of secondary hypertension due to, or associated with, severe renal disease, adrenal tumors, or pituitary basophilism. The final group consisted of 827 cases, the analysis of which constitutes the basis for our study. They were classified according to the method of Keith, Wagener, and Barker.[23] Group 1 included those patients who had only a mild narrowing or sclerosis of the retinal arterioles. Patients in Group 2 usually had moderate to marked sclerosis of the retinal arterioles, either of the chronic type characterized by exaggeration of the arterial reflex and arteriovenous compression, or of the postangiospastic type characterized by generalized and localized irregular narrowing of the arterioles. Patients who had hypertension, Group 3, had retinitis of the angiospastic type characterized by edema, cotton-wool patches, and hemorrhages in the retina, in combination with sclerotic and spastic lesions in the arterioles. Patients in Group 4 had edema of the nerve heads of the retinas, in addition to the retinal changes characteristic of hypertension, Group 3.

Two measurements of blood pressure were made in each case with a standard mercury sphygmomanometer. One was made during the clinical examination,* and one at the time of measurement of the basal metabolic rate.† All the patients had a systolic blood pressure of 150 mm. of mercury, or more, at the time of the clinical examination. The basal metabolic rates were measured by the technique outlined by

*Hereinafter referred to as clinical blood pressure.
†Hereinafter referred to as basal blood pressure.

TABLE I

DISTRIBUTION OF PATIENTS BY GROUP OF HYPERTENSION, SEX, AND AVERAGE AGE

GROUP	TOTAL	MALES	FEMALES
1	204	51 (38)*	153 (48)
2	437	109 (48)	328 (48)
3	146	60 (46)	86 (48)
4	40	19 (44)	21 (45)
Total	827	239	588

*The figures in parentheses indicate average age in years.

TABLE II

AVERAGE BLOOD PRESSURE IN EACH OF FOUR GROUPS OF HYPERTENSION

GROUP	BLOOD PRESSURE, MILLIMETERS OF MERCURY			
	CLINICAL*		BASAL†	
	SYSTOLIC	DIASTOLIC	SYSTOLIC	DIASTOLIC
1	172	102	150	90
2	208	124	174	106
3	225	140	191	120
4	243	156	212	139
Average	204	123	173	106

*Indicates blood pressure in the clinic.
†Indicates pressure at time that basal metabolic rate was measured.

TABLE III

AVERAGE BASAL METABOLIC RATE BY GROUP OF HYPERTENSION AND SEX OF PATIENTS

GROUP	AVERAGE BASAL METABOLIC RATE, PER CENT		
	TOTAL	MALES	FEMALES
1	+ 3	+4	+ 3
2	- 4	+4	+ 4
3	+ 5	+4	+ 6
4	+11	+8	+13
Average	+ 4	+4	+ 4

Boothby and Sandiford.[8, 24] Part of the clinical data are presented in Tables I and II. They do not require any comment.

The relationship of the basal metabolic rate to the hypertension in each group is shown in Table III and Fig. 1. The average metabolic rates in Groups 1 and 2 were essentially the same. The average rate of metabolism in Group 3 was slightly greater than that in Groups 1 and 2. The average rate of metabolism in Group 4 was about twice as much above normal as the average of Group 3 was above the normal. Considerable variability of metabolism was present in each group. Of the 204 patients in Group 1, fourteen had rates greater than plus 15 per cent (7 per cent), and, of these, two were greater than plus 20 per cent. In Group 2, thirty of the 437 patients had rates greater than plus 15 per cent (7 per cent), and, of this number, nine were greater than plus 20 per cent. In Group 3, seventeen of the 146 patients had rates greater than plus 15 per cent (12 per cent), and eight were greater than plus 20 per cent. Of the forty patients in Group 4, eleven had basal metabol-

ic rates in excess of plus 15 per cent (27 per cent), and four had rates greater than plus 20 per cent (Table IV). When the average basal metabolic rates of patients classified according to their basal systolic blood pressure are charted, there is shown to be a relationship (Fig. 2);

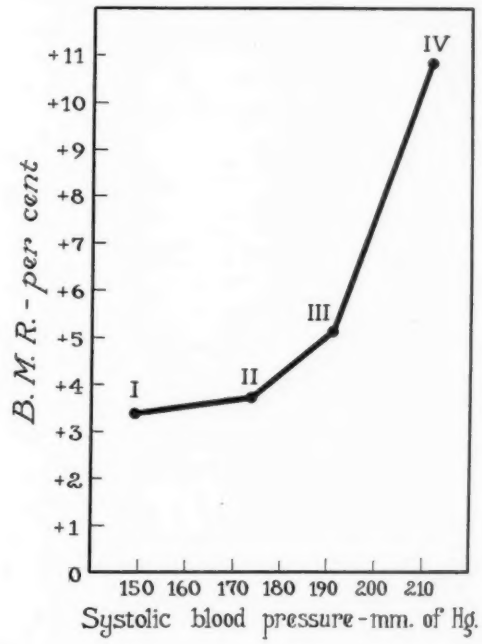

Fig. 1.—Average basal metabolic rates and basal systolic blood pressures of patients in each of four groups of hypertension.

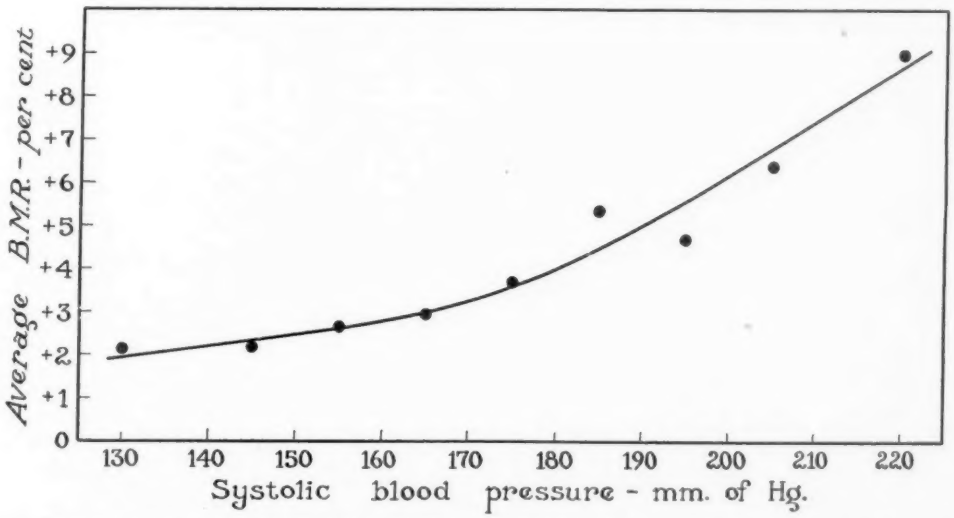

Fig. 2.—Average basal metabolic rates of patients classified according to their basal systolic blood pressures.

however, when individual cases are considered, there is shown to be very little correlation between basal metabolism and blood pressure (correlation coefficient = plus 0.2).

TABLE IV

PERCENTAGE DISTRIBUTION OF CASES IN EACH OF FOUR GROUPS OF HYPERTENSION ACCORDING TO BASAL METABOLIC RATE

BASAL METABOLIC RATE	PERCENTAGE OF CASES			
	GROUP 1	GROUP 2	GROUP 3	GROUP 4
Less than -15%	2	2	1	
-15% to +15%	91	91	87	73
Greater than +15%	7	7	12	27
Total	100	100	100	100

Most hypotheses relative to the elevated basal metabolism in essential hypertension involve the thyroid gland or the cardiac or respiratory systems. The basal metabolism tends to rise with the increased respiration associated with cardiac decompensation.[5, 25] Our patients were, however, as far as could be ascertained, free of dyspnea. Heart rate may, perhaps, influence the metabolism. Lev and Hamburger[26] studied a patient who could produce paroxysmal tachycardia at will, and found the basal metabolic rate to be minus 6 per cent with a pulse rate of 67, and plus 5 per cent when the pulse rose to 187. Our patients had essentially normal heart rates.

Some students of the subject have believed that the increased cardiac work resulting from the increased blood pressure might be the reason for increased metabolism in some cases of hypertension. Our data would seem to lend some support to this conclusion, for the average basal metabolic rate of all patients who had hypertension, Group 4, was higher than the average basal metabolic rate of all patients who had hypertension, Group 3, and these, in turn, had a higher average basal metabolic rate than patients who had hypertension, Group 2. We have shown that the average blood pressure of patients increases in each succeeding group (Table II). Thus, through hypertension Groups 1, 2, 3, and 4, there are a gradually increasing average blood pressure and gradually increasing average basal metabolic rate.

As indicated earlier, however, the correlation in individual cases is small. Further study of our cases is shown in Table V. Only patients who had a basal diastolic blood pressure of 130 mm. of mercury, or more, were included in Table V, for it was felt that hearts which were maintaining such high blood pressures were certainly overworking. In Group 3, only a fifth of the patients had a basal metabolic rate greater than plus 15 per cent, and, in Group 4, only about a third of the patients had basal metabolic rates exceeding plus 15 per cent. In other words, four-fifths of patients who have hypertension, Group 3, and diastolic blood pressures exceeding 130 mm. have metabolic rates which are within the accepted range of normal. Similarly, two-thirds of pa-

tients who have hypertension, Group 4, and diastolic blood pressures exceeding 130 mm. have basal metabolic rates within the accepted range of normal. If an increase of cardiac work had a marked effect on basal metabolic rate, probably more patients who have severe hypertension should have metabolic rates greater than normal. This evidence, we feel, shows the lack of marked relationship between an increased basal metabolic rate and cardiac work, per se.

TABLE V

DISTRIBUTION OF ALL CASES IN WHICH THE BASAL DIASTOLIC BLOOD PRESSURE WAS 130 MM. OR MORE, ACCORDING TO BASAL METABOLIC RATE

BASAL METABOLIC RATE	HYPERTENSION GROUP 3 (43 CASES)			HYPERTENSION GROUP 4 (25 CASES)		
	CASES	AVERAGE BASAL METABOLIC RATE	AVERAGE BASAL DIASTOLIC BLOOD PRESSURE	CASES	AVERAGE BASAL METABOLIC RATE	AVERAGE BASAL DIASTOLIC BLOOD PRESSURE
More than +15	8	+22	144	8	+22	147
0% to +15%	26	+ 8	135	16	+10	153
Less than 0%	9	- 5	130	1	- 7	130

In order to ascertain whether or not hypertension might provoke hyperthyroidism, microscopic sections of the thyroid glands of forty additional patients who had died of congestive heart failure due to hypertension were examined microscopically. In the forty cases studied there were none of the usual morphologic changes which are associated with hyperthyroidism. Kyser[27] was unable to find any more evidence of hyperthyroidism in thyroid sections of patients who had died of high blood pressure than in a control group. This is in accord with the results of others (Rose). Resnik and Friedman[28] have shown that congestion of the thyroid gland does not have any effect on the basal metabolism, as had been suggested by Lev and Hamburger.

We have noted a few instances in which partial thyroidectomy was done on patients who had severe hypertension and showed evidence of coexistent hyperthyroidism, but in whose thyroid glands no evidence of parenchymatous hypertrophy could be found. The elevated basal metabolic rate has not fallen appreciably after double resection of the thyroid glands in these cases. The increased metabolism was therefore linked with the hypertension.

In a recently examined series of sixty-nine patients who had essential hypertension and hyperthyroidism, in twenty-one cases the basal metabolic rate failed to fall as low as plus 20 per cent within two weeks of partial thyroidectomy, presumably because of hypertension. It is of interest that the average blood pressure readings both before operation and after operation were higher in these twenty-one cases than in the others. We have seen a number of patients who had hypertension and frank hyperthyroidism, in whom, after partial thyroidectomy with com-

plete relief of all clinical manifestations of hyperthyroidism, the basal metabolic rate has remained at levels greater than plus 20 per cent for years. In many of these patients the thyroid tissue which was removed showed the typical pathologic picture of exophthalmic goiter, but repeated periods of administration of iodine after the operation failed to lower the basal metabolic rate or alter the patient's clinical condition. This situation also seems to be due to hypertension.

We have observed a few instances of high-grade myxedema with associated severe hypertension in which repeated basal metabolic rates failed to be as low as minus 20 per cent. In three such cases that have come to our attention, administration of desiccated thyroid in quantities only sufficient to control the clinical evidence of myxedema has raised the basal metabolic rate to more than zero. It would seem likely, therefore, that the elevation of the basal metabolic rate in some cases of hypertension is probably independent of the thyroid gland or of excess thyroxin in the body tissues. The frequently repeated observation that elevated basal metabolic rates in many cases of hypertension will fall to normal levels after a few days' rest in bed also suggests that thyroxin is not present in excessive amounts.

It would seem logical to assume that the basal metabolic rate is elevated in some cases of hypertension because of inability of the patients to relax sufficiently to allow the test to be made under true basal conditions. It is admitted, however, that this explanation does not account for the failure of elevation of the basal metabolic rate in many other hypertensive patients who appear equally tense, nor do we feel that there is evidence to indicate that such a condition is necessarily the only factor tending to cause increased basal metabolic rates in some cases of hypertension. To our knowledge, no adequate explanation for this occurrence seems to be available. For the time being we can make no further observation than that hypertension and elevated basal metabolic rate are frequently associated in the absence of hyperthyroidism. The difficulty of differential diagnosis between hypertension with and without true primary hyperthyroidism makes further investigation of these patients important.

SUMMARY

A study of 827 cases of hypertension, in which thyroid disease was excluded as accurately as possible by clinical methods, showed that the basal metabolic rates were elevated, to higher levels and more frequently, in patients with higher blood pressures than in those with less marked hypertension. No adequate explanation of this phenomenon is apparent, although in our opinion the thyroid gland itself is not responsible.

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THE RELATIVE CLINICAL POTENCY OF DIGITALIS U.S.P. X, DIGITALIS U.S.P. XI, AND DIGILANID

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DIGITALIS therapy is based largely on the presumption that the various preparations in use are of known relative potency. Much difficulty has arisen, therefore, from the fact that the digitalis of U.S.P. XI (1936) is substantially more potent than that of U.S.P. X (1926), and that the precise difference in potency is still uncertain. The increase in strength of the official preparation of digitalis resulted from a change of the standard to which the drug is compared. Prior to 1936, digitalis was assayed in terms of ouabain. Since that time it has been made to conform in potency to the international standard powder adopted by the Health Committee of the League of Nations in 1925. The strength of the standard digitalis powder is such that 89.7 milligrams is the lethal dose per kilogram of cat. The "international digitalis unit" consists of 0.1 Gm. of the powder, and is the equivalent of 1.1 cat unit.

Judging from bio-assay by the frog and cat methods, the digitalis of U.S.P. XI appears to be from 25 per cent to 30 per cent stronger than that of U.S.P. X.[1] Clinical experience, however, has not yet demonstrated to what extent these figures are applicable to the therapeutic potency of digitalis. Bland and White[2] "suspect that in actual practice, an increase in potency up to 50 per cent is more nearly correct." Under the circumstances, it is desirable that the action of the newer preparation of digitalis should be carefully compared with that of the preparation previously in use in order to establish an accurate basis for modification of the prescribed clinical dosage. It is also of value to ascertain more precisely the relative strength of digilanid, a form of digitalis which has attracted recent attention because of the fact that it can be assayed chemically, thus assuring consistent potency. Digilanid is composed of the chemically pure glycosides of *Digitalis lanata*.

The following study presents a clinical evaluation of the potency of digitalis U.S.P. X, digitalis U.S.P. XI, and digilanid, in terms of the ability of these drugs to slow the ventricular rate in cases of auricular fibrillation. As will later be discussed, this action of digitalis is not identical with that by which the efficiency of ventricular contraction is improved or "toxic" effects are elicited. Conclusions as to digitalis potency which are based upon slowing of the ventricular rate in the presence of auricular fibrillation should not be compared without qualification to the results of assay by techniques which involve other functions of the drug.

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METHODS

Observations were made on a series of seventeen patients who had chronic auricular fibrillation and were under treatment in the Cardiac Clinic of the Philadelphia General Hospital. All patients were ambulatory. Their ages ranged from 32 to 69 years. Evidence of organic heart disease of rheumatic, hypertensive, or arteriosclerotic origin was present in all cases. The observations to be reported were made in the course of routine clinic visits at intervals of one to six weeks.

The routine consisted of digitalizing each patient with one of the three preparations studied, and thereafter giving a constant daily dose which was the same for all patients, irrespective of individual therapeutic indications. The daily dose of digitalis U.S.P. X (Upjohn) was 1½ grains (0.1 Gm.), of digitalis U.S.P. XI (Squibb), 1 grain (0.065 Gm.), and of digilanid (Sandoz), $\frac{1}{200}$ grain (0.3 mg.). When the ventricular rate had become stabilized, the studies described below were carried out. After the completion of study of each preparation, one of the others was substituted and the procedure repeated.

The criterion of potency of the drugs was the rate of contraction of the ventricles after a control period of rest in the seated posture and after exercise. The rate was counted first for one minute by auscultation. The patient then walked ten times over a two-step staircase, each step of which was 8 inches high. The patient selected his own pace, but was made to maintain it consistently in all subsequent tests. As the patient returned to his seat, the stethoscope was applied to his chest and the ventricular rate counted continuously from the moment he sat down until three minutes later; notation was made of the number of beats in each fifteen-second interval. A record was kept also of the room temperature and the patient's blood pressure, weight, and general condition, in order to eliminate factors which might render successive tests not comparable.

Electrocardiograms were recorded continuously before, during, and after exercise in several cases. From these it was apparent that the ventricular rate during the first fifteen seconds after exercise was the same as the maximum rate during exercise. Therefore, for the purposes of the present study, the rate during the first fifteen seconds of rest has been called the "maximum exercise rate."

The rate of the ventricles was the only objective criterion used in comparing the action of the three drugs. No account was taken of a pulse deficit, for estimates of this phenomenon are usually inaccurate, and are essentially an index of the tactile appreciation of the observer, rather than of any significant abnormality of circulatory function.

RESULTS

Comparison of digitalis U.S.P. X and digitalis U.S.P. XI was made in ten cases, of digitalis U.S.P. X and digilanid in sixteen cases, and of digitalis U.S.P. XI and digilanid in eleven cases. Table I summarizes the results obtained in ten cases in which all three preparations were compared on each patient. Because of differences between individual patients in their reaction to digitalis, only the cases included in Table I could be used as the basis for the following discussion. Confirmatory evidence, however, was afforded by the results obtained in the seven remaining cases, in which the effects of only two preparations were compared on each patient.

TABLE I

VENTRICULAR RATES IN TEN CASES OF AURICULAR FIBRILLATION, SHOWING THE RELATIVE EFFECT OF DAILY DOSES OF 1/3 MG. OF DIGILANID, 1½ GRAINS OF DIGITALIS U.S.P. X, AND 1 GRAIN OF DIGITALIS U.S.P. XI

(The rates were counted when the patient was seated [1] after rest, [2] during the first fifteen seconds after exercise, [3] during the first minute after exercise, and [4] during the second minute after exercise.)

PATIENT			DIGILANID				DIGITALIS U.S.P. XI				DIGITALIS U.S.P. X			
	AGE (YEARS)	ETIOLOGIC TYPES OF HEART DISEASE	REST	EXERCISE	1ST MIN.	2ND MIN.	REST	EXERCISE	1ST MIN.	2ND MIN.	REST	EXERCISE	1ST MIN.	2ND MIN.
1.	34	Rheumatic	83	136	118	88	78	128	112	87	72	128	97	74
			92	172	143	98	75	132	109	83	62	124	96	68
											72	132	114	81
		Average	88	154	131	93	77	130	111	85	69	128	102	74
2.	34	Rheumatic	54	132	108	66	72	128	104	72	49	116	90	67
			60	124	97	61	48	112	82	48	50	124	90	52
			49	120	93	57	60	108	95	65	44	96	77	54
			59	116	100	58								
		Average	56	123	99	61	60	116	94	62	48	112	86	58
3.	38	Rheumatic	68	144	118	78	57	132	100	62	60	120	89	60
			67	112	89	67	61	120	92	62	71	140	102	74
											57	132	104	57
		Average	68	128	104	73	59	126	93	62	63	131	98	64
4.	51	Rheumatic	92	136	120	102	77	124	105	79	80	124	104	87
			93	140	121	93	84	120	107	87	75	132	112	86
							80	140	107	82				
		Average	93	138	121	98	80	121	106	83	78	128	108	87
5.	50	Hypertension	75	140	121	89	86	112	98	87	75	124	104	83
			79	144	115	87	83	108	96	85	74	112	99	83
											74	120	106	84
		Average	77	142	118	88	85	110	97	86	74	119	103	83
6.	50	Hypertension	60	72	70	61	77	92	81	81	61	76	70	67
			62	80	74	65	82	100	87	84	64	80	75	66
			77	88	85	78					74	88	86	82
		Average	66	80	76	68	79	96	84	83	66	81	77	72
7.	58	Hypertension	72	124	102	74	79	112	100	87	88	132	119	93
			72	116	106	82	94	124	120	106	75	116	103	83
			81	132	115	83								
		Average	75	124	108	80	87	118	110	97	82	124	111	88
8.	69	Arteriosclerosis	83	136	111	93	81	108	98	84	85	124	107	90
			88	128	121	88	78	116	101	82	79	128	110	80
			71	104	95	80	81	116	103	81	80	124	107	83
		Average	81	123	110	87	80	113	101	82	81	125	108	84
9.	54	Arteriosclerosis	69	124	95	78	72	136	99	81	65	100	87	69
			45	84	76	50	45	116	85	59	60	120	92	69
			54	104	84	63	52	104	86	75				
		Average	56	104	85	64	56	119	90	72	63	110	90	69
10.	64	Arteriosclerosis	78	120	104	86	80	112	102	83	68	104	95	80
			73	100	91	83	71	116	98	76	70	100	90	76
			67	96	91	76	80	112	103	85				
		Average	73	105	95	82	77	113	101	81	69	102	93	78
Average of all patients			73	122	105	79	74	116	99	79	69	116	98	76

It is apparent from Table I that the same dose of digitalis does not necessarily produce the same ventricular rate in different patients. Thus, $\frac{1}{200}$ grain (0.3 mg.) of digilanid per day produced a ventricular rate at rest of 45 per minute in one patient and 93 per minute in another, and ventricular rates during exercise which varied from 72 to 172 per minute between different patients. This, of course, simply emphasizes the clinical experience that the optimum daily dose of digitalis, irrespective of its form or consistent potency, is not the same for all patients.

Comparing the two preparations of *Digitalis purpurea*, U.S.P. X, $1\frac{1}{2}$ grains (0.1 Gm.), and U.S.P. XI, 1 grain (0.06 Gm.), Table I shows that the average ventricular rates which they produced were remarkably similar. The average ventricular rate at rest produced by digitalis U.S.P. X was slightly slower than that produced by digitalis U.S.P. XI, but during and after exercise the two were practically identical. As to individual cases, four patients had a slightly lower rate when digitalis U.S.P. X was used, four had a slightly lower rate when digitalis U.S.P. XI was used, and two had approximately the same rate with either preparation. These results indicate that 1 grain (0.06 Gm.) of digitalis U.S.P. XI has an effect equivalent to $1\frac{1}{2}$ grains (0.1 Gm.) of digitalis U.S.P. X. The potency of digitalis U.S.P. XI is therefore 50 per cent higher than that of digitalis U.S.P. X in terms of slowing action on the ventricular rate in the presence of auricular fibrillation.

Comparing digilanid with *Digitalis Purpurea*, Table I shows that the effect on the ventricular rate at rest was the same for $\frac{1}{200}$ grain (0.3 mg.) of digilanid as it was for $1\frac{1}{2}$ grains (0.1 Gm.) of digitalis U.S.P. X or 1 grain (0.06 Gm.) of digitalis U.S.P. XI. The ventricular rate during exercise, however, averaged six beats per minute higher when digilanid was used than during the administration of either preparation of *Digitalis purpurea*. Presumably therefore, $\frac{1}{200}$ grain (0.3 mg.) of digilanid is slightly less potent in controlling the *rise in ventricular rate during exercise* than is $1\frac{1}{2}$ grains (0.1 Gm.) of digitalis U.S.P. X or 1 grain (0.06 Gm.) of digitalis U.S.P. XI.

It is customary in practice to modify the dose of digitalis to some extent in accordance with the patient's personal evaluation of such symptoms as breathlessness, palpitation, rapid or slow heart action, or nausea. The seventeen patients of this series were therefore asked from time to time whether they preferred digitalis or digilanid, and their reasons for so doing. Three preferred digitalis because they regarded it as "stronger" than digilanid. Four preferred digilanid because it was "easier to take" or "less nauseating" than digitalis. The remaining ten patients had no preference or changed their opinion so often that no significance could be attached to it.

Conspicuous differences between the three preparations in their "toxic" effects upon the heart were not apparent. The incidence of

premature contractions, as far as this could be judged by auscultation, did not seem to be influenced by changing from one preparation to another. There was likewise no basis for any definite conclusion as to the relative ability of the drugs to improve myocardial efficiency. The occurrence of signs of congestive heart failure did not have any obvious relationship to which particular preparation was used as long as the routine dosage was unchanged.

DISCUSSION

The data which have been presented constitute a basis for the evaluation of digitalis potency only in terms of effect on the ventricular rate in the presence of auricular fibrillation. The technique of study which was employed was not adapted to the accurate estimation of either the "toxic" action of digitalis or its therapeutic action in improving the efficiency of myocardial contraction.[3] Since the "toxic" effects may constitute an important factor in the bio-assay of digitalis by the frog or cat methods, it is easy to understand that estimates of digitalis by such standards may well differ from estimates based on the criterion of ventricular slowing. The same may be true also of the assay of digitalis in terms of its therapeutic effect in cases of normal sinus rhythm, when the drug action involves essentially the improvement of myocardial efficiency. The latter aspect of digitalis action is certainly the one most difficult to evaluate with accuracy, especially in cases of auricular fibrillation, in which ventricular acceleration plays an important role in the production of congestive phenomena. From the present study, the most that can be stated in regard to relative "toxic" effect (ectopic beats) or effect on the efficiency of myocardial contraction is that no conspicuous differences were observed between the results of a daily dose of $\frac{1}{200}$ grain (0.3 mg.) of digilanid, $1\frac{1}{2}$ grains (0.1 Gm.) of digitalis U.S.P. X, and 1 grain (0.06 Gm.) of digitalis U.S.P. XI.

The evidence which has been presented seems, on the other hand, to indicate with reasonable certainty that the relative potency of the three preparations in terms of slowing of the ventricular rate in the presence of auricular fibrillation is such that 1 grain (0.06 Gm.) of digitalis U.S.P. XI is exactly equal to $1\frac{1}{2}$ grains (0.1 Gm.) of digitalis U.S.P. X, and that the potency of $\frac{1}{2}$ grain (0.03 Gm.) of digilanid is slightly less than that of the other preparations. It is noteworthy that the difference in effectiveness of digilanid was apparent only during the exercise tolerance test. Judging from the ventricular rate when the patient was at rest, it might be assumed that no such difference existed. This fact illustrates a potential source of error when various forms of digitalis are compared and no account is taken of the rise in ventricular rate during exercise. It is evident from clinical experience that the resting ventricular rate in a case of auricular fibrillation is no indication whatever of the extent to which the rate increases during exercise.[4]

This acceleration of the rate during exercise is stated[5] to be due in the average case to decreased vagal tone. Conceivably, therefore, the fact that digilanid produced the same ventricular rate at rest as did digitalis, but permitted a greater increase in rate during exercise, may imply that the difference in potency between these preparations may involve only their vagal action. This possible qualitative distinction, however, is not supported by sufficient evidence from the present study to warrant its acceptance without further investigation.

CONCLUSIONS

1. Daily oral doses of 1 grain (0.06 Gm.) of digitalis U.S.P. XI, 1½ grains (0.1 Gm.) of digitalis U.S.P. X, and $\frac{1}{200}$ grain (0.3 mg.) of digilanid produced the same average ventricular rate at rest in cases of auricular fibrillation.

2. The degree of acceleration of the ventricular rate by exercise was the same when either of the two preparations of digitalis was given in the dosage stated above, but the degree of acceleration was slightly greater when digilanid was given.

3. Assayed in terms of their ability to slow the ventricular rate in cases of auricular fibrillation, 1 grain (0.06 Gm.) of digitalis U.S.P. XI is the equivalent of 1½ grains (0.1 Gm.) of digitalis U.S.P. X. The potency of digitalis U.S.P. XI is therefore 50 per cent higher than that of digitalis U.S.P. X.

4. The potency of $\frac{1}{200}$ grain (0.3 mg.) of digilanid is slightly less than that of 1 grain (0.06 Gm.) of digitalis U.S.P. XI, or 1½ grains (0.1 Gm.) of digitalis U.S.P. X.

5. Within the limited scope of this study, there was no evidence of any difference between the three preparations in either their "toxic" action or their influence on myocardial efficiency. It is emphasized, however, that the type of assay used is only accurate in evaluating the effect of digitalis on the ventricular rate in the presence of auricular fibrillation.

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Clinical Reports

RHEUMATIC THROMBOPHLEBITIS

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THE development of venous thrombosis in acute rheumatism has received various interpretations. Schmitt,[1] in 1884, expressed the view that thrombosis was the result of some alteration in the blood, rather than of an antecedent phlebitis. Gatay,[2] in 1895, described inflammatory changes in the vein wall and concluded that the thrombosis was entirely secondary to the associated phlebitis. Garnier[3] and others, however, regarded venous stasis as the main factor, but conceded that changes in the blood and in the vein itself may be contributory.

Poynton[4-6] reported extensive venous thrombosis in three children with rheumatic fever and subsequently observed ten additional cases of similar nature. In every instance there were manifestations of acute rheumatism at the time of thrombosis, a fact which the author considered presumptive evidence of active infection in the vein itself. Welch,[7] in 1900, agreed that phlebitis is a definite but uncommon complication of acute rheumatism. He considered the former of minor significance, however, in the causation of venous thrombosis in heart disease. In a review of twenty-eight cases complicating cardiac diseases in general, Welch found only three in which there was a history of recent joint symptoms. Sladen and Winternitz,[8] furthermore, have emphasized that any lesion of the heart resulting in congestive failure may be associated with venous thrombosis. In reviewing twenty-six rheumatic cases, they found that the interval between rheumatic fever and venous thrombosis varied from several months to many years; consequently, the authors were unable to establish that rheumatism was a definite etiological factor.

The histologic evidence that rheumatic foci occur within the venous system has likewise been inconclusive. In most instances, non-specific changes, in the nature of small round cell infiltrations and fibrosis of the vein wall, have been reported. Such alterations, obviously, may have been the result of venous thrombosis, rather than its cause. Perry,[9] however, in a case of acute rheumatic fever complicated by thrombosis of the right innominate vein, demonstrated, for the first time, lesions closely resembling Aschoff nodules in the media of the vein.

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The purpose of this paper is to record the second case of rheumatic thrombophlebitis in which the diagnosis was confirmed by histologic studies. It differs from the case of Perry in that other clinical and pathologic manifestations of acute rheumatism were absent, and, therefore, is unique.

CASE REPORT

J. S., a 39-year-old white Italian, a printer by occupation, was admitted to the hospital June 4, 1941, with the complaint of pain and swelling on the left side of the neck, shortness of breath on exertion, and swelling of the ankles. He had had typhoid fever, diphtheria, scarlet fever, and recurrent tonsillitis in childhood. In 1928 he suffered from painful joints, and, in 1937, had had a severe attack of influenza. In 1938 a diagnosis of mitral stenosis was made at this hospital when the patient was admitted for an unrelated cause. Shortness of breath on exertion had occurred intermittently since 1933, and, for two months prior to the present admission, dyspnea was marked even on walking a short distance on level ground. Swelling of the legs had been noted intermittently for a period of one month. On June 2, 1941, the patient experienced severe pain on the left side of the neck, followed, the next day, by swelling of the tissues in that area. He also complained of sharp pain on both sides of the chest on breathing, and of a cough productive of bloody sputum.

On physical examination, the patient appeared orthopneic, cyanotic, and toxic. His temperature was 100.4° F. The sclerae showed moderate icterus. There were tenderness and induration of the deep cervical nodes at the angle of the jaw on the left. Tender lymph nodes were palpated in the left supraclavicular region and in the left axilla. There were fullness and induration over the anterior triangle of the neck and in the supraclavicular and infraclavicular fossae on the left side. The breath sounds were diminished over the left infraclavicular region, and over both bases posteriorly there was dullness to flatness on percussion, with diminished to absent voice and fremitus, and many small moist râles on inspiration. The left border of the heart was 1½ cm. outside the left midclavicular line. The heart rate was 120 per minute, and the beat was regular except for occasional ectopic systoles. The blood pressure was 118/78. There was a mid-diastolic thrill over the apex. The heart sounds were fairly well transmitted, and there was a snapping first sound at the mitral area, with an accentuated pulmonic second sound. There was gallop rhythm at the tricuspid area, and a diphasic friction rub, synchronous with systole and diastole, was heard over the precordium. No definite murmur could be made out. The liver was four fingerbreadths below the right costal margin in the midclavicular line, and was smooth and tender. The spleen was two fingerbreadths below the left costal margin, and had a firm, round edge. There was moderate ankle and pretibial edema. The impression at this time was rheumatic heart disease, with mitral stenosis and congestive failure, and thrombophlebitis of the left internal jugular vein, with multiple infarcts in both lungs.

A roentgenogram of the chest showed that the cardiac shadow was enlarged in the transverse diameter and also toward the back, obliterating the retrocardiac space in the region of the left auricle and ventricle. The maximum heart measurements were 5.7 cm. to the right and 11.4 cm. to the left; the transverse diameter of the chest was 30.4 cm. The general appearance suggested mitral valvular disease. Multiple, dense shadows were scattered throughout both lungs, particularly the lower lobes; these were regarded as infarcts (Fig. 1).

The electrocardiogram showed a sinus tachycardia of 120 per minute. There were marked right axis deviation and inversion of the T wave in Lead IV. The P-R interval and QRS time were within normal limits.

The blood Wassermann and Kahn reactions were negative. Urine analysis showed nothing abnormal. The nonprotein nitrogen of the blood was 45 mg. per cent.

The icterus index was 25. On June 5, 1941, the erythrocyte count and hemoglobin were normal. There were 9,200 leucocytes, of which 83 per cent were neutrophiles. On June 13, 1941, the leucocyte count was 25,500, with 84 per cent neutrophiles. A blood culture was negative.

While in the hospital, the patient continued to have a low-grade fever, and showed little response to digitalization and mercurial diuretics. The swelling in the left supraclavicular and infraclavicular regions subsided to a large degree, and a firm, tender, cordlike structure was palpable beneath the left sternomastoid muscle. The cough became more frequent, and there were copious expectoration of bloody sputum and severe pain in the lower ribs. The patient became stuporous, lapsed into a muttering delirium, and died June 17, 1941.

The autopsy was performed by Dr. J. G. Pasternack, pathologist.

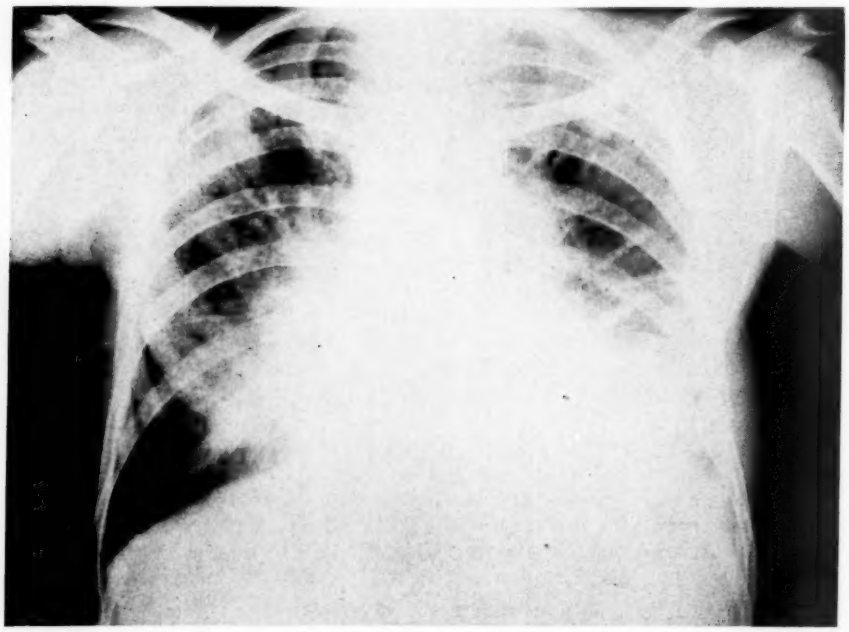

Fig. 1.—Roentgenogram of chest, showing multiple infarcts throughout both lungs.

The body was fairly well developed and nourished. There was a moderate degree of jaundice of the skin and sclerae. The left side of the neck showed fusiform bulging along the sternomastoid muscle. The peritoneal cavity was half filled with clear, straw-colored fluid. The liver was enlarged, firm, and smooth; the spleen was large and firmly adherent to the diaphragm. There were no adhesions to the sternal plate. The right lung was massively fixed in place by old adhesions which formed cystic spaces containing large quantities of hemorrhagic fluid. The left side of the chest was half filled with bloody fluid. The pericardial sac was greatly distended, and contained approximately 250 cc. of faintly turbid, straw-colored fluid.

The heart weighed 680 grams. The right atrium was approximately three times the normal in size, and the left atrium was probably ten times the normal in size and extremely thin. The pulmonary and tricuspid valves were normal. The musculature of the right ventricle averaged 8 mm. in thickness. The mitral orifice was markedly stenosed; it admitted an instrument ½ cm. in diameter with difficulty. The mitral cusps were entirely replaced by old, deforming scar tissue and organized vegetations which were rough and hemorrhagic in appearance. At the

base of the valves there was marked calcification. The chordae tendineae were markedly sclerosed, as were the apices of the papillary muscle. The musculature of the left ventricle averaged 24 mm. in thickness. The aortic orifice was markedly stenosed; its circumference was slightly more than 3 cm. The cusps were adherent and greatly deformed by scar tissue. Their bases showed old sclerosis and calcification. The coronary ostia were deformed and stenosed as a result of advanced atheromatous changes in the aorta. The coronary arteries were patent.

Fig. 2.—Dissection showing massive thrombosis of left internal jugular vein.

There was massive thrombosis of the left internal jugular vein from the base of the skull to its junction with the left subclavian vein (Fig. 2). It was 5 cm. in diameter in its largest part. The thrombotic process extended for a short distance into the left innominate and subclavian veins, and also involved the thoracic duct. The thrombus in the internal jugular vein in its most distal portion was well organized, and inseparably fused with the wall of the vein for a distance of about 1 cm. upward. Beyond this point the organization was recent, and the thrombus could be separated from the vessel wall. The blood clot was apparently old.

The lungs together weighed 1,550 grams. The pleural surfaces showed old and recent fibrosis. Numerous firm infarcts were present in all the lobes of both lungs. On section, infarcts of various sizes, from less than 1 cm. to masses 6 cm. by 10 cm., were found throughout both lungs. Some were old and partly organized; others were red and hemorrhagic, and apparently of recent origin. The liver weighed 2,300 grams. On section the hepatic parenchyma showed an advanced nutmeg appearance.

Fig. 3.—Wall of vein, showing acute Aschoff nodule.

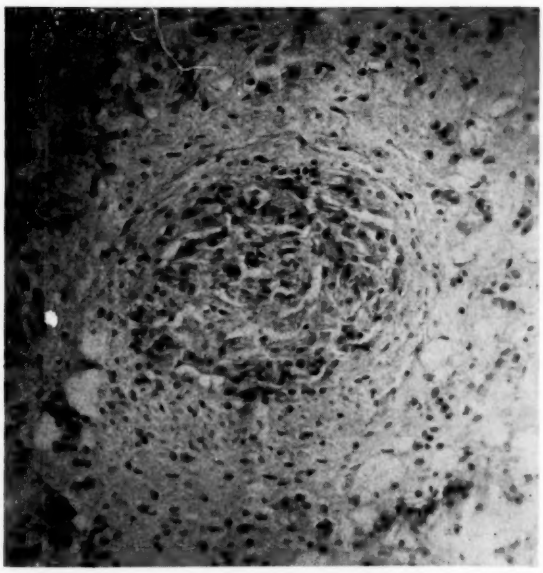

Fig. 4.—Wall of vein, showing fibrosing Aschoff nodule.

The anatomic diagnosis was chronic rheumatic valvulitis, mitral and aortic, massive thrombosis of the left internal jugular vein, multiple infarcts of both lungs, old and recent, bilateral fibrosanguinous pleuritis, chronic pleuritis on the right, hydropericardium, and hydroperitoneum.

MICROSCOPIC EXAMINATION

There were extensive areas of old and recent infarction in the lungs, and, in some sections, necrotic parenchyma in the process of suppuration could be seen. The heart showed old endocardial and pericardial fibrosis. No fresh vegetations were found on the heart valves. There were extensive, irregular, interstitial fibrosis and foci of old scarring in the myocardium.

The internal jugular vein showed massive thrombosis and thrombophlebitis. The normal architecture of the wall was entirely destroyed. The inflammatory reaction varied in different areas. Stretches of the intima showed thrombonecrosis and merged inseparably with the thrombus. In certain areas there was a granulating endophlebitic reaction, with more or less marginal organization of the thrombus. The media and adventitia showed extensive, active fibroplasia, fibrosis, and capillary vascularization. Here and there the vasa vasorum and capillaries showed fibrinous and fibrinopurulent thrombosis, massive thrombonecrosis, and granulating and fibrosing thromboangiitis, with recanalization or complete occlusion of the lumen. In some areas small blood vessels showed fibrinoid degeneration of their wall and perivascular fibroplasia, with dense infiltrations of plasma cells, monocytes, and eosinophiles. There were occasional, small, pseudogranulomatous foci formed of hypertrophied fibroblastic cells, plasma cells, and lymphocytes. A small central blood vessel, showing fibrinoid degeneration or fibrosis of its wall, was usually present. In other similar lesions the associated blood vessel showed fibrosing pseudogranulomatous panangiitis, with perivascular fibroblastic mantling and infiltration of plasma cells, monocytes, and eosinophiles. These lesions were regarded as fibrosing Aschoff nodules. Some of the nodules were more typical than others (Figs. 3 and 4).

COMMENT

Most authors have hesitated to accept the occurrence of venous thrombosis in rheumatism as secondary to definite phlebitis of rheumatic nature. This has been particularly the case when the thrombosis was observed as an incident to an apparently quiescent stage of the disease. Welch, among others, considered recent joint symptoms or active endocarditis essential to the diagnosis of rheumatic phlebitis, and, since he found a low incidence of both in his series, minimized the role of rheumatic infection. Sladen and Winternitz, likewise, believed that rheumatic phlebitis should be closely related to the active rheumatic state. Nevertheless, the chronicity and recurrent nature of rheumatism led them to acknowledge the possibility of a persistent focus within the vein which might ultimately lead to thrombosis. This concept is strengthened by the observations in our case, in which active carditis was absent at autopsy and joint symptoms had preceded venous thrombosis by many years.

Although it is true that venous thrombosis is a not infrequent complication of congestive heart failure, the latter is not a primary factor in all rheumatic cases. Remlinger[10] has described a case of extensive venous thrombosis associated with acute articular rheumatism, without carditis.

Voelcker[11] likewise observed involvement of the femoral and saphenous veins in a case of chorea without apparent heart disease. These observations, together with the histologic changes described herein and previously recorded by Perry, indicate that rheumatic infection, per se, may be responsible for venous thrombosis.

It has been shown that the entire arterial system, from the aorta to the smallest of its ultimate divisions, may be involved by the virus of acute rheumatic fever.[12, 13] The recognition of specific rheumatic lesions in the venous system tends further to emphasize the fact that widespread vascular damage may occur in this disease.

SUMMARY

1. A case of massive thrombosis of the left internal jugular vein complicating rheumatic heart disease is presented.

2. The histologic changes indicate that thrombosis was secondary to a definite phlebitis of rheumatic nature.

3. The absence of other clinical and pathologic signs of acute rheumatism strongly suggests that active infection persisted within the vein wall long after the acute phase of the disease had passed. The occurrence of venous thrombosis months or years after acute rheumatism, therefore, does not necessarily exclude the possibility of an underlying rheumatic phlebitis.

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POLYPOID THROMBUS OF THE LEFT AURICLE, WITH REPORT OF A CASE

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DETROIT, MICH.

THE recent literature[1, 2, 3] furnishes a few case reports of tumor masses of the auricles, most of which have been accepted as myxomas arising from the auricular septum. In the following case report the history is similar to that of previously reported myxomas, but the anatomic interpretation differs from that of other reported cases.

CASE REPORT

The patient entered the University Hospital* April 16, 1941, complaining of weakness, difficulty in walking, and speech defects. Since the patient was unable to speak distinctly and, in addition, understood and spoke English poorly, the history was not complete. The symptoms apparently began four months before the patient's admission to the hospital; first there were stiffness of the left hand and pain in the left shoulder. Then a speech defect developed; it was noted that the patient seemed to drag his words. During the second month of his illness the patient had two periods of unconsciousness; the nature of the attacks was not known. In the following months some disability of his upper extremities developed. No further history was obtained.

Physical examination revealed that the patient was not acutely ill. The temperature was 98° F., the pulse rate, 80, the respiratory rate, 20, and the blood pressure, 104/78. A marked arcus senilis was present. The pupils were slightly irregular, reacted slowly to light, and were constricted. The fundi were normal. A loud presystolic murmur was heard over the precordium; it was loudest at the apex and along the left sternal border. A thrill could be palpated at the apex of the heart. Moist inspiratory râles were noted at the bases of the lungs. Abdominal and rectal examination was negative. A hydrocele was present on the right.

Neurologic examination revealed that the patient responded slowly and poorly. He walked slowly, with a broad base, but there was no evidence of hemiparesis. The extraocular movements were normal save for a slight nystagmus on looking to the right. The right angle of the mouth was pulled back less than the left, and there was some smoothing of the face. The tongue protruded in the midline and was not atrophied. The reflexes of the biceps and triceps were exaggerated bilaterally, but more on the left. Hoffman's sign was positive on the left. There was some clubbing of the fingers, and there was marked spasticity of both upper extremities. The knee jerks were hyperactive, particularly on the left. The Babinski sign was negative.

Routine laboratory examinations showed that the blood, the urine, and the stool were normal. The sedimentation index was 1.63 mm./minute, with a hematocrit reading of 34 per cent. The electrocardiogram showed a small, notched QRS complex in all leads. Roentgenologic examination revealed that the skull was negative. Cardiac enlargement was present, and a minimal degree of infiltration was noted in each apex.

No diagnosis was made of the neurologic condition, and the patient was trans-

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ferred to the medical service for treatment of his suspected mitral rheumatic heart disease. The patient was digitalized and maintained on a dose of 0.1 Gm. of digitalis daily. On this medication the moist râles in the lungs cleared up. The final diagnosis was cardiac enlargement caused by mitral stenosis. Rheumatic fever was the suspected cause of the valve defect. Function was judged to be grade I. The patient was discharged from the University Hospital April 27, 1941, and advised to continue taking digitalis.

The patient was admitted to St. Mary's Hospital, Detroit, Aug. 27, 1941. It was learned from informants that the symptoms had become aggravated in the preceding four days. Information concerning the patient's course during the interval could not be obtained, and the patient was too ill to question.

Examination on admission to the hospital revealed a poorly nourished, extremely ill person. The temperature was 99° F., the pulse rate, 96, and the respiratory rate, 20. The blood pressure was not recorded. The patient was dyspneic and cyanotic. The pupils reacted poorly to light. Numerous coarse râles were heard over both lungs. The heart was enlarged to percussion, but no murmurs were heard. The patient had pronounced dependent edema and some ascites. The reflexes were hypoactive. The patient failed rapidly, and died several hours after his admission to the hospital.

NECROPSY EXAMINATION

The autopsy was performed ten hours after death. The body was that of a well-developed, rather poorly nourished, white man. Mild pitting edema of the lower extremities was present. Approximately 2,000 c.c. of clear serous fluid were found in the peritoneal cavity. There were 1,500 c.c. of serous fluid in the left pleural cavity and approximately 500 c.c. in the right. The pericardial sac showed no abnormalities.

The heart measured 16 cm. in its greatest width. The weight of the unopened heart, containing the tumor and a few blood clots, was 560 grams. Examination of the descending branch of the left coronary artery revealed a moderate degree of sclerosis, but no points of occlusion could be detected. The recurrent branch and the right coronary arteries were normal in appearance. The ventricular muscle was flabby, and examination of the surface made by cutting revealed in the inferior half of the left ventricle numerous fibrotic patches measuring from 2 mm. to 5 mm. in diameter. No recent infarcts were seen. The root of the aorta was smooth; the right auricle and the right auricular appendage were normal.

Examination of the left auricle showed that it was bulbous in character, and portions of a tumor mass protruded from the cut ends of the pulmonary veins. The auricle was markedly dilated. Since the nature of the tumor was obvious, the left ventricle was opened and the tumor inspected through the mitral valve. It was seen to hang into the valve when the heart was suspended, and to slide to and fro in the auricle when the heart was manipulated; this movement might have occurred during the life of the patient. The left auricle was carefully opened along its lateral surface, and a soft, pale yellow, gelatinous tumor was seen almost filling the chamber. From the more firm central portions of the tumor, soft, friable, papillary processes protruded; many of these were easily broken from the tumor, even though it was handled gently. The entire mass was adherent by a narrow pedicle to the auricular wall approximately 3 cm. superior to the mitral valve. The tumor mass measured approximately 10 cm. in its widest diameter and about 4 cm. in thickness. Further examination of the heart revealed that all chambers were dilated. The valves were normal in appearance, and the vena cava, which was opened in its entirety, was also normal.

The right lung weighed 790 grams, and the left, 619 grams; their pleural surfaces were smooth, and both organs were brownish in color. A large amount of fluid exuded from their cut surfaces, and several infarcts were seen in the lower lobes. The liver weighed 1,824 grams, and examination of its cut surface revealed

a marked degree of chronic passive congestion. The total weight of the kidneys was 303 grams. Their cut surfaces appeared congested, and a well-defined infarct was seen in the superior pole of the right kidney. The remainder of the organs were normal. Unfortunately, permission to examine the brain could not be obtained.

The tissues were fixed in a 10 per cent solution of formalin and were stained with hematoxylin and eosin, Weigert's elastic tissue stain, van Gieson's stain, and Wilder's silver stain. In addition, several stains were used for mucin, including thionin, mucihematin, and Lillie's toluidine methylene blue.[4]

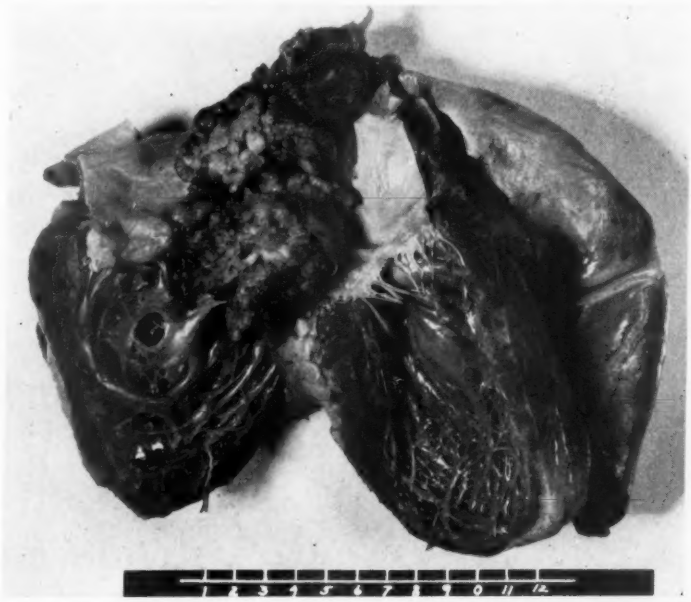

Fig. 1.—Polypoid tumor of opened auricle.

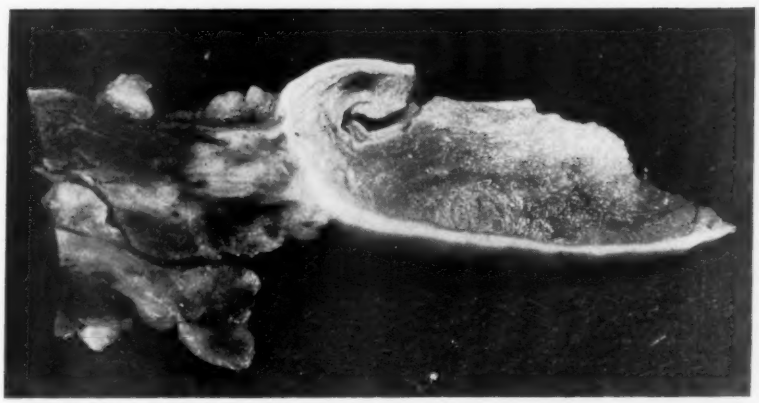

Fig. 2.—Section through septum. Note connective tissue bands extending from rounded auricular wall.

Examination of paraffin sections of the tumor showed that its papillary processes were covered by endothelium. In the hematoxylin and eosin stains the bulk of the tumor stained lightly with eosin and was relatively acellular. The stroma was interrupted by many irregular vascular channels, and many vacuoles were seen at

various points. Closer examination showed that the stroma was formed by delicate eosin-staining fibers embedded in a grayish ground substance. A few giant cells of the foreign body type hugged the vascular channels, and many erythrocytes and a few lymphocytes were noted here and there in the stroma. In the matrix there were a few large cells which were spindle-shaped and had large elliptical nuclei, with a moderate amount of chromatin. The cytoplasm of these cells was difficult to distinguish in most instances. Numerous macrophages filled with an iron-containing pigment were present throughout the entire tumor, but more were seen near and about the pedicle.

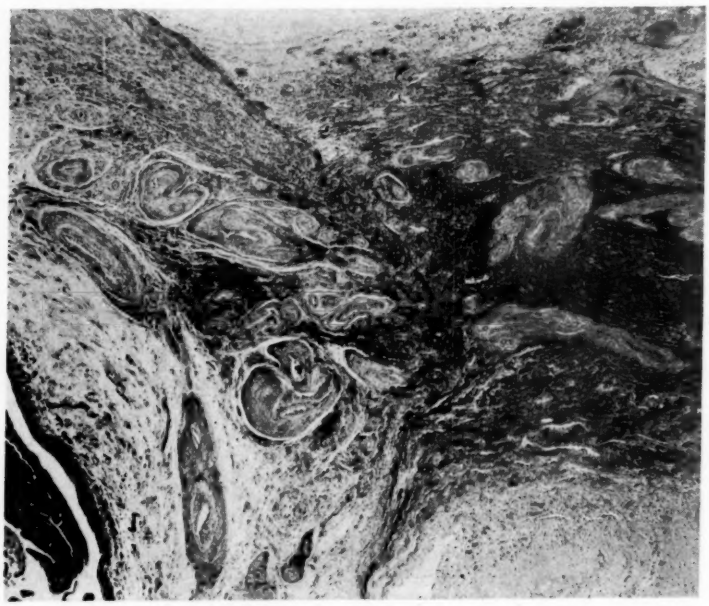

Fig. 3.—Section through pedicle. van Gieson's stain. ×25.

Several sections taken directly through the pedicle revealed a marked increase in collagenous tissue immediately beneath the endocardium. Here there was a surprisingly large number of arterioles of various sizes, the smallest of which showed marked subintimal hyaline deposits, and the larger of which showed extensive intimal thickening, with almost complete closure of their lumens. In the latter vessels the picture was that of disuse atrophy. Numerous collagenous fibers were seen in the pedicle, and were found to be continuous with those of the auricular wall and to extend as armlike processes into the tumor. Many of the dense areas of collagenous fibers were separated by looser, somewhat myxomatous, tissue. Small arterioles in the proximal portions of the pedicle were also present. In the deeper portions of the pedicle, approximately 1 cm. from the auricle wall, the tumor was made up of looser connective tissue separated by myxomatous portions of the stroma.

Reticular fibers were abundant throughout the tumor, but only a few, fine, elastic fibers were seen in sections stained by Weigert's method. The specific stains failed to give a positive reaction for mucin.

Examination of sections taken from the left ventricle revealed an increase in connective tissue beneath the endocardium. In many areas the myocardial fibers were replaced by collagen, and several recently healed infarcts were noted. The myocardial fibers appeared to be increased in diameter. The smaller branches of the coronary artery showed irregular intimal thickening. No evidence of rheumatic heart disease was apparent.

Sections of the lungs and liver showed advanced chronic passive congestion, and there were large areas of necrosis about the central veins of the liver. Sections of the spleen and kidneys revealed a moderate degree of passive congestion. No changes were noted in the small arterioles of the kidneys.

Fig. 4.—Section taken from periphery of tumor. Hematoxylin and eosin stain. ×25.

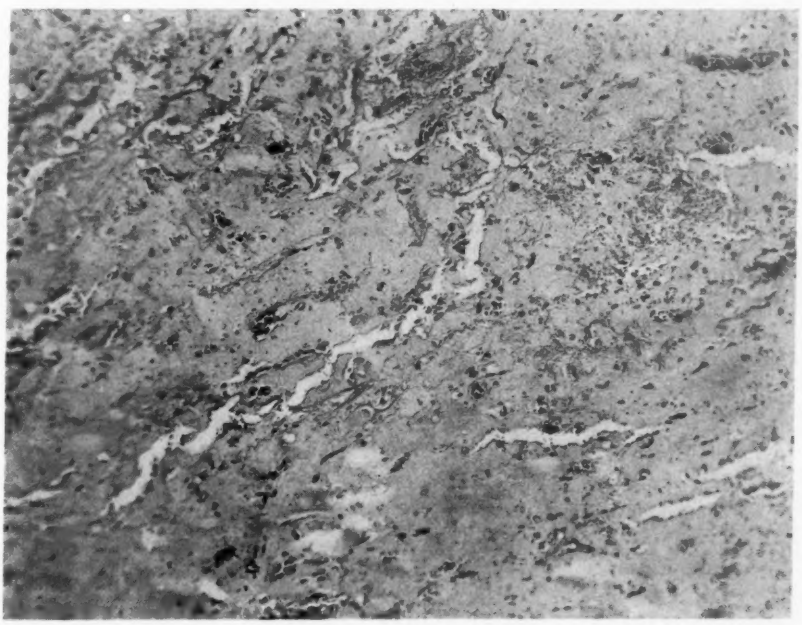

Fig. 5.—Section taken from periphery of tumor. Hematoxylin and eosin stain. ×100.

DISCUSSION

Examination of this tumor indicated that the mass was not a myxoma, but was a pedunculated mural thrombus undergoing organization and retrogressive changes. The following is the evidence in favor of this thesis.

1. The observed coronary sclerosis, myocardial fibrosis, and cardiac hypertrophy, accompanied by congestive heart failure, may explain the formation of a thrombus.

2. The presence of injury to the auricular wall at the site of attachment of the pedicle is suggestive of a pedunculated mural thrombus.

3. The arteries of the auricular wall showed disuse atrophy, which would not be expected if a myxoma were growing from this site.

4. The structure of the pedicle and the central portion of the mass was that of an organizing thrombus, whereas the bulk of the tumor showed retrogressive changes.

5. The tumor failed to show the histologic features of a myxoma, nor did it give the characteristic stains for mucin.

The differences between organized thrombi and true myxomas have been discussed in several publications.[1] In the majority of the previous case reports, detailed studies of the pedicles of the tumors have not been recorded, but coronary sclerosis, with areas of myocardial fibrosis, has been seen.[2] Since the history and the gross appearance of the tumor were similar to the history and gross appearance in many previously described cases, it is possible that some of the auricular masses may not be true myxomas. Careful study will probably show that many pedunculated tumors of the auricles are, as Warthin has shown,[5] organizing thrombi.

SUMMARY

1. A primary tumor of the left auricle is reported.

2. Anatomic studies of the tumor would indicate that the mass was an organizing thrombus originating from the interauricular septum.

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ELECTROCARDIOGRAMS SIMULATING THOSE OF CORONARY THROMBOSIS AFTER CESSATION OF PAROXYSMAL TACHYCARDIA

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NEW HAVEN, CONN.

THE occurrence of transient abnormalities of the T wave of the electrocardiogram after the cessation of paroxysmal tachycardia has recently been emphasized by Campbell[1] in a report of several instances in which some flattening, and even inversion of this deflection was noted for days after paroxysms, in subjects who gave no other evidence of cardiovascular disease. The earliest allusion to such phenomena appears to be that of Graybiel and White,[2] who briefly mentioned two instances in a report dealing with inversion of the T waves associated with a variety of essentially noncardiac disorders.

We have encountered such abnormalities on two occasions in a subject whose several electrocardiographic abnormalities were so extreme in degree and prolonged in duration that the case was considered sufficiently remarkable to be placed on record.

CASE REPORT

M. T. (Unit No. 18626), a 38-year-old policeman, ate a large dinner of corned beef, cabbage, and turnips, and immediately afterward developed epigastric distress, together with rapid beating of the heart and a mild smothering sensation. His symptoms, which persisted throughout the night, were not sufficiently disturbing to prevent his spending the evening out with friends and indulging in several highballs and a midnight luncheon, but he slept poorly after retiring. The next morning he visited his doctor, who administered a white pill every three hours, but the tachycardia persisted all day, and the patient grew sufficiently uncomfortable to apply for admission to the New Haven Hospital, on Jan. 25, 1932.

The patient had not had similar symptoms before, and he had always considered himself in vigorous health. He smoked in excess of a package of cigarettes daily.

Examination in the hospital revealed a youthful-appearing man with slight cyanosis of the lips, hands, and feet. The neck veins were slightly distended in the sitting position. The heart sounds were of good quality, but the rate was extremely rapid, and a pulsation synchronous with the heart beat was visible in the epigastrium. The blood pressure was 95/80. The edge of the liver reached about 3 cm. below the costal margin. A few râles were heard in the base of the right lung. The electrocardiogram confirmed the clinical impression of paroxysmal tachycardia; the ventricular rate was 230 (Fig. 1, *A*). The leucocyte count was 13,800, with 80 per cent polymorphonuclear cells. The temperature was 101° F. by rectum.

Pressure upon the carotid sinus region, eye balls, and epigastrium did not influence the heart rate, and vomiting induced by ipecac was also ineffectual. Quinidine sulfate was administered orally, therefore, in a test dose of 0.2 Gm., followed by another dose of 0.2 Gm. in ninety minutes. A third dose of 0.4 Gm., given three

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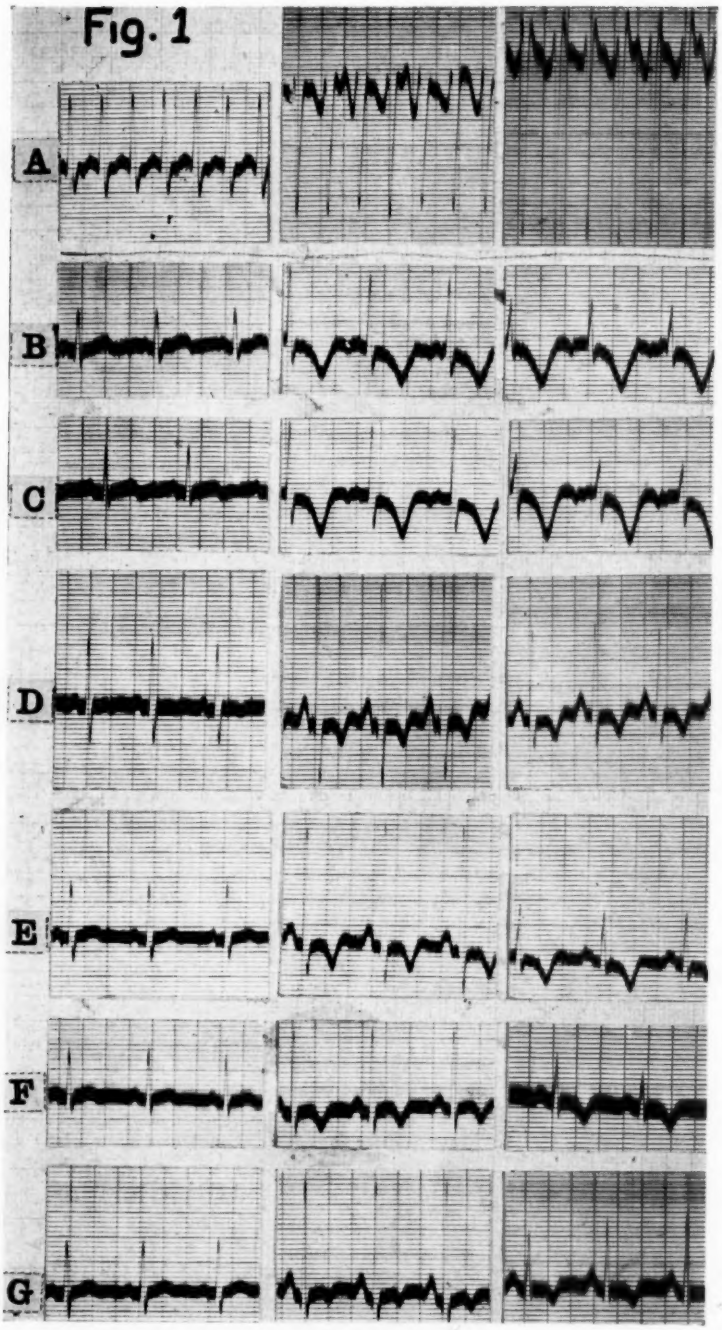

Fig. 1.—Leads I, II, and III from left to right. *A* shows paroxysmal tachycardia with a rate of 230; the paroxysm lasted about forty-four hours. *B* and *C* were obtained on the first and second days, respectively, after termination of the paroxysm, and *D*, *E*, *F*, and *G* were obtained on the ninth, sixteenth, twenty-third, and thirty-seventh days, respectively, after termination of the attack.

hours later, was followed in about an hour by sinus rhythm with a rate of 100. This terminated a paroxysm that had lasted about forty-four hours. Within a few hours all the symptoms and the physical abnormalities had disappeared, the blood pressure was 125/85, the leucocyte count had fallen to 8,750, with 50 per cent polymorphonuclear cells, and the temperature had become normal.

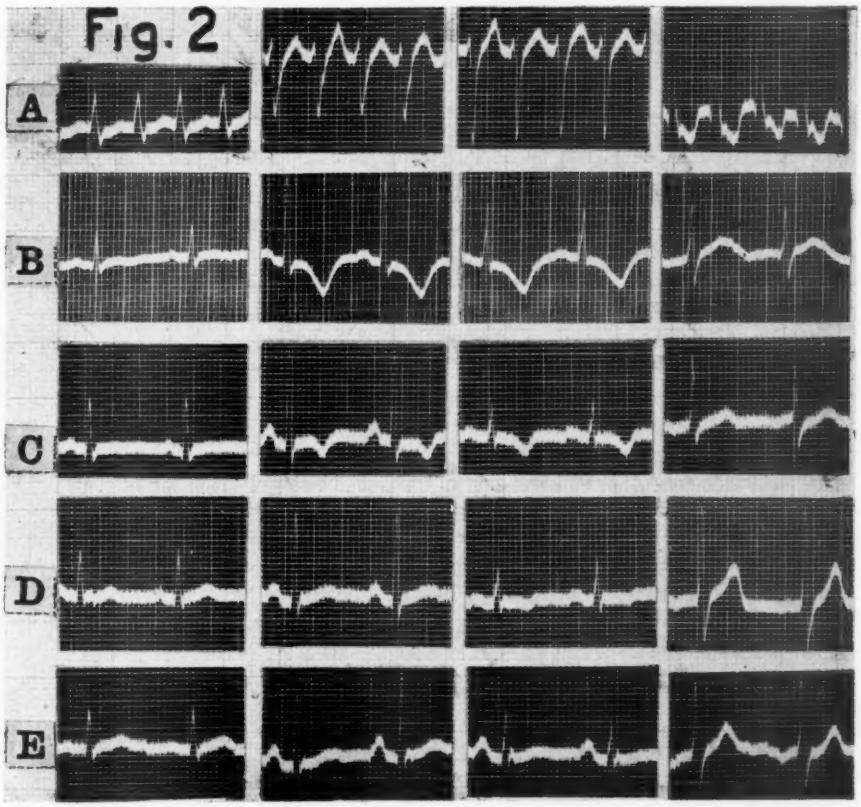

Fig. 2.—Leads I, II, III and IV F from left to right. *A* shows paroxysmal tachycardia with a rate of 200; the paroxysm lasted at least nine hours (not longer than nineteen). *B* was obtained within an hour of termination of the paroxysm, and *C*, *D*, and *E* were obtained twelve, twenty-six, and forty days later.

Just prior to the patient's discharge, on the following day, a routine electrocardiogram was obtained (Fig. 1, *B*), and this unexpectedly revealed T waves of an unusually wide and deeply inverted contour in Leads II and III, with slight depression of the associated RS-T segments; additional features of interest were low amplitude and deformity of the P waves, and abnormally long Q-T duration: the value for "K" was 0.509, as against the normal maximum value of 0.392.[3] Although the electrocardiographer raised the question of coronary thrombosis, the patient had already left the hospital, and insisted on continuing his normal activity, for he felt entirely well. He agreed, however, to present himself for follow-up examinations, and during the ensuing thirty-five days the five additional electrocardiograms shown in Fig. 1 were obtained. It is noteworthy that abnormalities of the T waves persisted throughout this period, but the depth of the inversion diminished gradually, the P waves became prominent upright deflections, and the Q-T duration regressed to the low normal value of 0.34 for "K."

Ten years later, on the morning of Sept. 25, 1942, the patient walked into the emergency room with another paroxysm of tachycardia which had been present on arising that morning. He complained only of palpitation and faintness. Except for two brief attacks of palpitation several years before, he had been in seemingly excellent health during the decade between visits. The blood pressure was 95/60, the edge of the liver was several centimeters below the costal margin, and a few râles were heard in the base of the right lung. The electrocardiogram (Fig. 2, *A*) confirmed the diagnosis of paroxysmal tachycardia of supraventricular origin. Again, after several hours of rest, during which repeated trials of the usual pressure maneuvers failed to terminate the paroxysm, 1 Gm. of quinidine sulfate was given in divided doses over a period of about three hours. Within half an hour after the last dose, and not less than nine hours after the onset of the paroxysm, normal sinus mechanism suddenly returned, and the patient was quickly relieved of his symptoms and signs. Again, the posttachycardia electrocardiogram (Fig. 2, *B*) showed pronounced inversion of the T waves in Leads II and III, with flattening in Lead I; and again the P waves were deformed and the Q-T duration abnormally long, with "K" equal to 0.535.

The patient was discharged the same day, and advised to take 0.2 Gm. of quinidine three times daily for two days. He returned to work immediately, but again cooperated in a protracted electrocardiographic follow-up study of his case. The three records subsequently obtained at fortnightly re-examinations over a forty-day period again showed persistence of the abnormalities for at least twelve days, with ultimate restoration of normal P and T waves and Q-T segments in the tracing taken on the twenty-sixth day after the paroxysm (Fig. 2). The patient continued asymptomatic and actively at work. The blood pressure was consistently about 115/75, the heart remained normal to auscultation, and the cardiac configuration and size were still normal on fluoroscopic examination at the time of the last electrocardiogram.

COMMENT

Because auricular paroxysmal tachycardia is encountered commonly in young adults, often under conditions of stress, but usually in the absence of demonstrable heart disease, its relatively frequent occurrence in military and wartime industrial life is to be anticipated. Since the more severe attacks draw attention to the heart, and may sometimes simulate coronary thrombosis clinically, the fact that the electrocardiogram may be grossly abnormal for days and weeks after the attack may mislead the physician into a diagnosis of a grave myocardial lesion; in fact, one of Campbell's cases was that of a member of the Royal Air Force who had been hospitalized for six weeks under the suspicion of "myocarditis."

The striking prominence and depth of the T-wave abnormalities and their long persistence after acute cardiac attacks might readily lead to an erroneous diagnosis of myocardial infarction, with the imposition of an unnecessarily long convalescence, the pronouncement of a needlessly bad prognosis, and perhaps ill-advised retirement from active service. That such a diagnosis is untenable in the case described would appear certain from the fact that the patient had no cardiovascular symptoms whatever in the ten years between the two recorded attacks,

that the clinical course after each attack was not that of acute coronary thrombosis, and that the normal electrocardiographic pattern was not only entirely restored, but was regained in too short a time for myocardial infarction to have occurred; moreover, detailed study of the abnormal records reveals certain differences between them and the classical picture of acute myocardial infarction, such as *depression* of the RS-T segments in the leads with inverted T waves, and failure of abnormal Q waves to develop.

How may these extraordinary abnormalities be explained? Although quinidine is known to produce changes in the final deflection of the ventricular complex, the brief exhibition of the drug and the small doses given this patient cannot account for the persistence of the abnormalities over a period of weeks. One may offer the hypothesis that the changes resulted from myocardial ischemia associated with a sharply diminished cardiac output during the many hours of the unusually high ventricular rate of the paroxysms. A common antecedent factor in the few reported instances of these strange effects has been the relatively long duration of the paroxysm that preceded them. A causal relationship to time is suggested by the observation in our case that the abnormalities regressed about twice as rapidly after the second paroxysm, which was less than half as long as the first. The persistence of the abnormalities for several weeks would seem to imply that some injury to the heart muscle had occurred, but the ultimately complete electrocardiographic and clinical recovery suggests that the injury was of a reversible nature, and did not lead to death of tissue. Whatever the true explanation, the evidence at hand would indicate that the electrocardiographic developments represent a transient and probably benign incident associated with paroxysmal tachycardia, and their recognition should prevent a too ready and dogmatic diagnosis of coronary thrombosis.

Last, but not least, another cause for inversion of T waves must be added to the already long but still growing list.

SUMMARY AND CONCLUSIONS

Pronounced electrocardiographic abnormalities simulating myocardial infarction, and lasting for several weeks, were encountered in two series of electrocardiograms taken after attacks of paroxysmal tachycardia in a man who appears to have no structural disease of the heart. The abnormalities probably represent benign, functional changes, and they should not be mistaken for evidence of coronary thrombosis. The observations add another item to the list of causes for abnormal T waves.

ADDENDUM

Since the acceptance of this paper for publication, two other relevant reports have come to the author's attention. The first was that of P. Cossio and his associates (Rev. argent. de cardiol. **8**: 168, 1941), and

the other was a case report by G. M. Currie (Brit. Heart J. **4**: 149, 1942). Of the five patients described, one died, and necropsy revealed some cardiac dilatation but no abnormality of the coronary vascular system and no focal myocardial lesions.

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Abstracts and Reviews

Selected Abstracts

Essex, H. E., Herrick, J. F., Mann, F. C., and Baldes, E. J.: The Effect of Atropine on the Coronary Blood Flow of Trained Dogs With Denervated and Partially Denervated Hearts. Am. J. Physiol. **138**: 683, 1943.

In the present study, the response of the coronary blood flow and heart rate to atropine sulfate has been observed after the following operative procedures: (1) right and left sympathetic ganglionectomy from the eighth or ninth intercostal space anteriorly, including the stellate ganglion; (2) double vagotomy in the neck; (3) a combination of procedures 1 and 2. In the absence of the sympathetic nerves, as in procedure 1, atropine caused increases of 25 to 85 per cent in coronary flow, and an increase in pulse rate of a similar magnitude. Atropine was without effect on the coronary blood flow, heart rate, or blood pressure of vagotomized animals, or animals with denervated hearts. It may be concluded that the increased coronary blood flow following injections of atropine is not owing to a direct effect of the drug on the wall of the blood vessel, nor is it due to changes of blood pressure. The augmented coronary flow follows the inhibition of vagal tone, and is associated with the resulting increased cardiac rate. When all of the evidence is considered, it is difficult to escape the conclusion that the increased heart rate itself is responsible for the increased coronary blood flow following administration of atropine, but the mechanism by which it is accomplished is not apparent.

AUTHORS.

Pochin, E. E.: Edema Following Ischemia in the Rabbit's Ear. Clin. Sc. **4**: 341, 1942.

If the circulation to the rabbit's ear is arrested for eighteen hours and then released, massive edema develops within two hours.

The edema may subside in a few weeks, or, when ischemia has been at a higher temperature or has been of longer duration, it may terminate in dry gangrene.

The protein concentration in the edema fluid is initially about 5 per cent, but falls progressively.

AUTHOR.

Levy, H., and Boas, E. P.: Angina Pectoris and the Syndrome of Peptic Ulcer. Arch. Int. Med. **71**: 301, 1943.

Certain relations between the syndromes of angina pectoris and peptic ulcer are described. It is suggested that neurogenic mechanisms mediated by the vagus nerve are concerned in this association.

AUTHORS.

Garvin, C. F.: Cardiac Cirrhosis. Am. J. M. Sc. **205**: 515, 1943.

Of 790 consecutive, adult, autopsied patients who died of heart disease, thirty-five (4.4 per cent) had cardiac cirrhosis. Only those cases were included in which there was actual architectural distortion of the liver.

Cardiac cirrhosis occurred essentially in two types of heart disease, viz., rheumatic heart disease (fourteen of 119 cases), and hypertensive heart disease (fourteen of 264 cases).

From a clinical standpoint, there was a tendency for the cases of cardiac cirrhosis to be associated with multiple episodes of failure, ascites, splenomegaly and, in the rheumatic group, with tricuspid stenosis. In five of the thirty-five cases studied, the diagnosis was suspected clinically. It appears that there are no definite criteria, however, which permit the consistent clinical diagnosis of cardiac cirrhosis.

AUTHOR.

Cooke, W. T., and White, P. D.: Paroxysmal Ventricular Tachycardia. Brit. Heart J. 5: 33, 1943.

The authors have reported twenty-seven cases of ventricular paroxysmal tachycardia. Twenty-four of these were found in a review of 51,000 plates and films taken on about 25,000 patients in the Cardiographic Laboratory of the Massachusetts General Hospital, over a period of twenty-five years, from 1914 to 1939.

The criteria for diagnosis were the electrocardiographic findings. Fulfillment of any one of the following four points justifies the diagnosis.

1. The presence of P waves at a slower rate than that of abnormal QRS waves during the paroxysm of tachycardia.

2. A paroxysm of abnormal ventricular complexes, that is, three or more, occurring during auricular fibrillation.

3. The onset of tachycardia with an abnormal ventricular complex.

4. Close resemblance of the complexes of ventricular premature beats to the complexes occurring during paroxysmal tachycardia.

Coronary heart disease was present in twenty-two of our twenty-seven cases; four had apparently normal hearts; and one was thought to have a congenital ventricular septal defect. There were seventeen males and ten females, the youngest being aged 18 years and the oldest eighty-one years.

Digitalis had been administered to thirteen of the twenty-seven cases before the onset of tachycardia. It was probably the chief etiological factor in at least five of these cases.

It is suggested that abnormalities of the ventricular complexes of premature beats are responses to stimuli arising in the A-V node or bundle or main branches, at a point in the cardiac cycle when the conducting tissues are still partially refractory. The onset of ventricular tachycardia was generally in the part of the cycle that has been associated with the supernormal phase. The mechanism of ventricular tachycardia with alternating complexes may be due to abnormalities in conduction along the bundle branches in response to impulses arising in the A-V node.

The prognosis is generally, but not always, poor. Only two patients with coronary heart disease survived longer than two years from the first attack. Five patients with hearts otherwise normal have survived to date, periods varying from two to fifteen years.

Quinidine or quinine should be used in adequate dosage in the treatment of the attack, being given either by mouth, intramuscularly, or intravenously. Quinidine sulfate is most conveniently given by mouth in the dosage of 6 to 9 grains every two hours for five to six doses, under close observation and preferably with electrocardiographic control. If quinidine fails, quinine dihydrochloride, grains 7½ subcutaneously, every two hours, is recommended to stop the paroxysm, and even to save life. A daily maintenance dose of quinidine by mouth (3 grains of the sulfate, four times a day) may be continued for prophylactic purposes for an indefinite time.

AUTHORS.

Ungerleider, H. E., and Gubner, R.: Extrasystoles and the Mechanism of Palpitation. Tr. Am. Therap. Soc. 41: 1, 1942.

An analysis was made of 1,142 cases with extrasystoles in order to determine their clinical significance. In 58 per cent, no objective evidence of heart disease was found.

Ventricular extrasystoles occur with considerably greater frequency than supraventricular premature contractions, and in the presence of heart disease there is a still greater preponderance of ventricular premature contractions.

Several factors, which are discussed, increase the significance of premature beats. Among these are the occurrence of premature beats of multifocal origin; frequent and persistent premature beats, particularly if they occur successively in short runs interrupting the regular rhythm; a definite increase in the number or shower of extrasystoles immediately following exercise; occurrence of premature contractions in the presence of a rapid heart rate; inversion of the T wave in the regular beat which follows the extrasystole; and postextrasystolic pulsus alterans.

Palpitation is a very common symptom often associated with extrasystoles. It has been generally attributed to an increased forcefulness of the regular beat following the premature systole, but several reasons are presented which indicate that this explanation is not tenable. It is suggested that palpitation occurring with premature contractions or tachycardia is due to, or associated with, an increased intensity of the first heart sound resulting from a more forcible closure of the arterioventricular valves. The symptom of palpitation is of no particular significance, and occurs in normal subjects as well as in those with heart disease.

AUTHORS.

Campbell, M.: Partial Heart Block With Dropped Beats. Brit. Heart J. 5: 55, 1943.

Partial heart block with dropped beats is nearly always transient, so that it is rare to find a patient in whom this rhythm can be expected as a usual or even a common finding.

At one time or another it was observed in nearly one-sixth of a series that included all types of heart block, but this gives an exaggerated idea of its frequency because it was generally transient and of short duration.

In two-thirds of the cases (twenty-five out of thirty-eight) there was a known cause, active infection or treatment with digitalis. In fourteen the cause was an acute infection, in five it was treatment with digitalis, and in six both causes combined. As would be expected, acute rheumatism was the most common infection (nine of twenty cases); but tonsillitis, without any suggestion that it was rheumatic, was often found.

The patients with dropped beats due to infections were mostly between 18 and 34 years of age. The outlook in this group was surprisingly good and the patient often recovered, even to the stage of a normal P-R interval. As an exception, the simultaneous association of tonsillitis and hyperthyroidism with dropped beats seemed of grave significance.

In the remaining third (thirteen cases) there was chronic heart disease and no very obvious reason why the dropped beats should have been found at the time they were, for here, too, they were generally transient. These were older patients, nearly all well over 60 years of age: all had chronic heart disease; high blood pressure and coronary atheroma were each the etiological factor in one-third, and in the remaining third there was myocardial disease without evidence of either of these factors.

In addition, some degree of heart block generally remained in the group of older patients, half of them having 2:1 heart block as a common or as their most usual rhythm. This was not so with the younger patients. Complete heart block also was uncommon in the group of younger patients with infections, but was present at some time in about one-fourth of the older group. The regular sequence of dropped beats, 2:1 heart block, and, finally, complete heart block were observed, but were rare.

The length of the P-R intervals was also studied. Progressive lengthening, but with a decreasing increment, was the rule, the increase of the second P-R interval over the first being much larger than the subsequent increases. There were, however, exceptions. In about one-eighth of the cases with dropped beats, these came without any gradual lengthening of the P-R interval (Hay's depression of excitability); these patients were mostly older ones with chronic heart disease.

For each grade of heart block up to a dropped beat after six responses, there were enough records to give some average figures, which are as follows:

3:2 heart block; 0.23, 0.35 second, dropped beat
4:3 heart block; 0.23, 0.30, 0.35 second, dropped beat
5:4 heart block; 0.23, 0.285, 0.32, 0.35 second, dropped beat

It must, however, be repeated that these are only the average of figures that varied widely in the different cases. It is strange that the average and the range of the P-R intervals between the first response after and the last response before the dropped beat should be so constant, whether there is one dropped beat to three, four, five, or six responses. This finding and some of the other points that have been discussed suggest that the defect of conductivity is generally the condition which makes heart block likely, but that something else, probably excitability, decides if there will be block, and, if so, of what grade it will be.

AUTHOR.

Carrillo, E. G.: A Fatal Case of Tachycardia and Paroxysmal Dyspnea in an Infant. Rev. argent. de cardiol. **9**: 247, 1942.

The observation is recorded of an infant whose death, after a few hours of illness, seemed to be due to acute pulmonary edema. A great cardiac acceleration to 214 per minute was present clinically, and electrocardiographically resembled supraventricular paroxysmal tachycardia.

AUTHOR.

Walker, C. W.: Pregnancy and Labor in a Case of Congenital Coarctation of the Aorta. Brit. M. J. **1**: 190, 1943.

The decision to allow labor to continue rather than have early recourse to cesarean section was prompted by the following considerations: The patient felt strong and well, was calm and confident, and was anxious to make the attempt; the infant was small and its presentation normal (L.O.A.), so that its passage might reasonably be expected to be an easy one; the early progress of cervical dilatation was free from fatigue and cardiac distress. In spite of these favorable circumstances the labor had to be stopped as soon as second-stage pains set in, as it was obvious that the tension in the upper circulation was being dangerously raised. With a full-term child, a less favorable presentation, a maternal heart having less reserve, or in the presence of more distressing first-stage pains, the danger point might well be reached before dilatation was complete and delivery possible. This being so, it would appear that in cases of coarctation of the aorta, however favorable, the obstetrical procedure of choice is cesarean section at the onset of labor.

AUTHOR.

Hansen, A. E., Platou, R. V., and Dwan, P. F.: Prolonged Use of a Sulfonamide Compound in Prevention of Rheumatic Recrudescences in Children: An Evaluation Based on a Four-Year Study on Sixty-Four Children. Am. J. Dis. Child. 64: 963, 1942.

A sulfonamide compound (sulfanilamide or, in a few instances, sulfathiazole or sulfadiazine) was administered to 53 different children for a total of 78 season cases to determine their value in preventing the occurrence of active rheumatic cycles, and the results were compared with those observed in 32 control children followed for a total of 46 season cases. All subjects studied were between 3 and 16 years of age, and had had essentially similar histories as regards previous rheumatic episodes, degree of cardiac involvement, and social status. These children were observed under conditions which closely approximate those encountered in the private practice of medicine. Only two of the 53 children in the group treated with a sulfonamide compound experienced a rheumatic flare-up, and in one this occurred within six days after the use of the drug was begun. On the other hand, 17 of the 32 children in the control group had a total of 21 rheumatic recrudescences. Eight of these recurrences were considered moderately severe; seven were mild, and in six of the subjects attacks of chorea were noted. In addition, the treated patients seemed favorably affected as regards the trend in degree of cardiac involvement, size of the heart, and functional classification. No difference was noted in the number of infections of the upper respiratory tract in the two groups, whereas the treated patients as well as the patients in the control group gained, and from a clinical viewpoint tended to be in better condition. Toxic manifestations due to the drug and disturbances in blood cells were seldom encountered, although during the fourth season the use of sulfathiazole was discontinued for one patient when the number of leucocytes dropped to 1,700. Improvement in the electrocardiographic tracings, though suggestive in several instances, could not be attributed to the effects of the drug alone. There was no evidence that the sulfonamide compounds produced changes in the electrocardiograms which may have been interpreted as being deleterious.

Although this series of cases is relatively small, the results are consistent, and, when interpreted in the light of observations of other investigators on this subject, appear to justify further study of the practical value of sulfonamide compounds in preventing rheumatic recrudescences. This appears to be especially true when we are aware that this disease is one of the major causes of disability and death in children of school age in the temperate zone. Caution should be the rule, and each child so treated should be under the care of a scrutinizing physician at all times.

AUTHORS.

Hansen, A. E.: Conditions Causing Confusion in the Diagnosis of Rheumatic Fever in Children: Analysis of Diagnoses Made by Practicing Physicians in 271 Rheumatic Subjects. J. A. M. A. 121: 987, 1943.

In the attempt to determine which disorders in children tend to be confused diagnostically with rheumatic fever, a study was made of the diagnoses given by practicing physicians and resident staff members with regard to 271 children with rheumatic fever who were admitted to the inpatient and outpatient cardiac disease clinic of the Department of Pediatrics of the University of Minnesota from 1928 to 1941. There was essential agreement in diagnosis in two-thirds of the cases. Review of the records of the remaining cases revealed that the conditions which caused most difficulty in the diagnosis of rheumatic fever under these conditions were: abdominal pain with possible appendicitis (about one-fourth of the cases studied); acute anterior poliomyelitis; acute osteomyelitis; erythematous or purpuric skin eruptions;

evidences of acute nephritis; acute fulminating illness (sepsis, pneumonia, subacute bacterial endocarditis); low-grade infections; and nervousness in mild chorea minor.

In order that the advantage gained by the early diagnosis and treatment may be realized to the fullest extent, the physician who is called on to care for children should be thoroughly familiar with the various and diverse manifestations of rheumatic fever.

AUTHOR.

Quinlan, J. T.: Sudden Death in Unsuspected Rheumatic Carditis. Brit. M. J. 2: 695, 1942.

A case of rheumatic carditis occurring in an apparently healthy infant, age 2 years, 8 months, is recorded. The post-mortem examination of the heart showed general enlargement as well as rheumatic mitral and tricuspid valvulitis. The finding of characteristic Aschoff bodies was accepted as proof of the rheumatic nature of the infection, and the other components of the microscopic picture provided additional evidence in support of this conclusion.

MCCULLOCH.

Roberts, J. E., and Lisa, J. R.: The Heart in Pulmonary Tuberculosis: A Clinico-Pathological Study of 100 Autopsied Patients. Am. Rev. Tuberc. 47: 253, 1943.

The findings in a clinico-pathological study of the heart in 100 cases of active pulmonary tuberculosis are presented. Demonstrable myocardial lesions were present in sixty-nine. They consisted of tuberculous myocarditis in ten, acute rheumatic myocarditis in one, Aschoff body-like lesions in nine, acute interstitial myocarditis in fifty, and acute miliary infarctions in eleven. Combinations of the lesions were found in thirteen. Healed rheumatic valvulitis was found in five, sclerotic lesions of the mitral and aortic valves in twenty, acute valvular endocarditis in two, and syphilitic aortic valvulitis in two. There were three instances each of tuberculous, chronic adhesive, and acute nontuberculous pericarditis. Tuberculous myocarditis was more frequent in the adults than in the children. Nontuberculous pulmonary infections appeared to be a significant factor in the causation of the interstitial myocarditis. Miliary infarctions occurred predominantly in the hypertrophied hearts, in hearts with severe coronary arteriosclerosis, and in the later decades of life. The conception of a small heart in tuberculosis was not substantiated. Right ventricular hypertrophy was very uncommon. Mensuration of the ventricular wall appeared to be an unreliable criterion for hypertrophy; the microscopical appearance of the myocardial fibers appeared more accurate. A moderate or severe disproportion between pulse rate and height of temperature was suggestive of myocardial disease. Murmurs due to organic valvular lesions were fairly common. Functional murmurs were uncommon. The conception that hypertension and active tuberculosis are incompatible was not borne out. Electrocardiographic tracings frequently revealed significant observations. While the present series is too small to permit definite conclusions about many controversial points, it is the belief of the authors that more attention paid to the cardiovascular system in the tuberculous individual will result in a more accurate estimation of existing cardiac damage.

AUTHORS.

Suzman, S.: Tuberculous Pericardial Effusion. Brit. Heart J. 5: 19, 1943.

A case of tuberculous pericarditis is described. It is suggested that in any obscure case of pericardial effusion, especially where this is large, tuberculosis should be thought of as a possible diagnosis, and that this is still more likely if tapping has to be repeated.

Among 1,893 consecutive autopsies there were six cases of tuberculous pericarditis, but only one of these had been diagnosed clinically. Hemopericardium did not occur in any of these cases. Some excess of pericardial fluid was found in about one-fourth of all the tuberculous cases.

AUTHOR.

Goldblatt, H., Kahn, J. R., and Lewis, H. A.: Studies on Experimental Hypertension. XIX. The Production of Persistent Hypertension in Sheep and Goats. J. Exper. Med. **77**: 297, 1943.

Persistent hypertension has been produced in the goat and sheep by constriction of the main renal arteries. The presence or absence of accompanying uremia depends upon the degree of constriction of the renal arteries.

In both sheep and goat, constriction of one main renal artery also caused elevation of the blood pressure, which tended to persist longer than in the dog. Excision of the one kidney with main renal artery constricted resulted in a prompt (twenty-four-hour) return of the blood pressure to normal.

In the animals with hypertension of long duration but without renal excretory insufficiency (the "benign" phase) no significant arterio- or arteriolosclerosis developed as a result of the hypertension alone. In the animals that had both hypertension and renal excretory insufficiency (the "malignant" phase) the typical terminal arteriolar lesions developed in many organs. These lesions consisted of necrosis and fibrinoid degeneration of arterioles and necrotizing arteriolitis which should not be confused with arteriolosclerosis.

The same humoral mechanism which is responsible for experimental renal hypertension in the dog and other animals also obtains in the pathogenesis of experimental renal hypertension in the sheep and goat.

AUTHORS.

Goldblatt, H., Katz, Y. J., Lewis, H. A., and Richardson, E.: Studies on Experimental Hypertension. XX. The Bioassay of Renin. J. Exper. Med. **77**: 309, 1943.

A simple, rapid method for the bio-assay of renin has been presented. Reliable and consistent results are obtained by this method whereby an arbitrary dog unit of renin has been established.

The response of normal unanesthetized dogs to renin is independent of the body weight of dogs weighing between 10 and 25 kilograms. An estimate of potency of renin per kilogram of body weight of the test animals is therefore not only unnecessary but misleading.

A dog unit of renin has been defined as that amount which raises the blood pressure at least 30 and not more than 35 mm. Hg within three minutes, in at least three unanesthetized dogs. The potency is expressed as dog units of renin per cubic centimeter.

The determination of the amount of renal substance represented by a cubic centimeter of extract and the number of dog units per cubic centimeter give an estimate of the yield of renin which can be expressed as dog units of renin per gram of original renal tissue.

By determination of the number of dog units per cubic centimeter and the amount of nitrogen in milligrams per cubic centimeter in any renal extract, the purity of the renin can be determined and expressed as dog units of renin per milligram N.

The establishment of a standard method for the bio-assay of renin is considered highly desirable, and the method outlined in this paper is suggested for this purpose.

AUTHORS.

Foà, P. P., Woods, W. W., Peet, M. M., and Foà, N. L.: Effective Renal Blood Flow, Glomerular Filtration Rate and Tubular Excretory Mass in Arterial Hypertension. II. Effect of Supradiaphragmatic Splanchnicectomy With Lower Dorsal Sympathetic Ganglionectomy. Arch. Int. Med. 71: 357, 1943.

Diodrast and inulin clearances were used to measure the effective renal blood flow and filtration rate in seventeen patients with arterial hypertension. Measurements were made before bilateral supradiaphragmatic splanchnicectomy with lower dorsal sympathetic ganglionectomy, and from two weeks to twelve months after the operation. The results indicate that the operation did not change the renal blood flow significantly, even when the blood pressure was reduced. There was a reduction of blood pressure in eight patients. Constancy of renal blood flow, combined with reduced blood pressure, suggests decreased vascular resistance and intrarenal arteriolar vasodilatation, with a resultant increase in pulse pressure within the kidney.

The patients with the highest effective renal blood flow, the greatest vasomotility, and the least thickening of the systemic arterioles received the most benefit from the operation. It is suggested that the determination of effective renal blood flow, and the measurement of the wall/lumen ratio of the systemic arterioles in biopsy specimens of muscle, might prove to be valuable in the preoperative study of patients with arterial hypertension.

The authors' results are consistent with the hypothesis that reduced intrarenal pulse pressure, and not renal ischemia, is a causal factor in human hypertension.

AUTHORS.

Pickering, G. W., Prinzmetal, M., and Kelsall, A. R.: The Assay of Renin in Rabbits With Experimental Renal Hypertension. Clin. Sc. 4: 401, 1942.

Extracts of rabbit kidneys made by three different methods have been assayed for their renin content by finding the amount raising the unanesthetized rabbit's blood pressure to the same extent as a given dose of a standard preparation. The standard was stable for at least two and one-half years.

The renin content of normal rabbits' kidneys shows considerable variations, the causes of which are undetermined, although higher values tend to occur in rabbits that are immature than in those that are fully grown.

When hypertension is produced by constricting the renal artery in the rabbit, the renin content of the kidney depends on the degree of constriction and on the duration of the hypertension. When the constriction is severe enough to produce renal necrosis, the hypertension is fleeting, and after one to two days the renal renin content is abnormally low. When the constriction is severe enough to produce hypertension within twelve hours, but not to produce renal necrosis, the hypertension is maintained, and in the first eight days the renal renin content tends to be abnormally high. When hypertension has lasted two to seventeen months, the renal renin content is normal.

By a method of extraction described in the text renin can be recovered from blood ten to fifteen minutes after its intravenous injection. None has been recovered from the blood of rabbits with hypertension of two to five months' duration.

The results obtianed are consistent with the hypothesis that the hypertension which occurs in the first few days after constricting the renal arteries is due to the release of renin from the kidney. The normal renal content of animals with prolonged hypertension suggests that factors other than the enhanced secretion of renin may contribute materially to the genesis of prolonged hypertension after renal artery constriction. These factors have not yet been identified.

AUTHORS.

Hass, G. M.: Elastic Tissue. III. Relations Between the Structure of the Aging Aorta and the Properties of the Isolated Aortic Elastic Tissue. Arch. Path. **35**: 29, 1943.

It is not possible to predict the mechanical or dynamic behavior of isolated elastic networks from knowledge of the behavior of the aortic wall from which they are obtained. The average purified networks are more extensible than the intact aorta. The extensibility is greatest among young networks, and usually increases with age, but occasional aged elastic systems have the characteristic high extensibility of youthful tissue.

The low extensibility of aged dilated intact aortas is partly due to the fact that at zero load the elastic networks are under tension. When the constraints responsible for this constant tension are removed, the elastic networks spontaneously retract to the dimensions of an undilated aorta.

After removal of mechanical or chemical forces, either of which may produce near maximum extension, all purified elastic systems, irrespective of age, exhibit identical and almost perfect retraction.

The tensile strength of isolated networks is, as a rule, high in the early decades, and low in the late decades of life. When elastic systems with low tensile strength are encountered in middle life, peculiar crystal patterns abutted by collagenous splints are found in the axes of elastic lamellae. Elastic systems with low tensile strength in late life have conspicuous discontinuities but not axial crystals. The evidence indicates that some of these discontinuities arise by disintegration of elastic lamellae at focal points of collagenous splinting and axial crystallization. The genesis of these medial changes and their contribution to the formation of atherosclerotic lesions remain obscure.

AUTHOR.

Bartol, G. M., Edwards, J. E., and Lamb, M. E.: Mycotic and Dissecting Aneurysms of the Aorta Complicating Bacterial Endocarditis. Arch. Path. **35**: 285, 1943.

The case of a 75-year-old man with acute bacterial endocarditis of the aortic valve, in whom a dissecting aneurysm of the aorta arose in the base of a complicating mycotic aneurysm, is presented.

The etiological organism was a pleomorphic gram-negative lactose-fermenting bacillus that could not be classified accurately.

The case is unusual from several angles, namely, (1) the association of bacterial endocarditis with dissecting aortic aneurysm, (2) the development of dissecting aneurysm in the base of a mycotic aneurysm, and (3) the type of organism responsible for the endocarditis.

AUTHORS.

Bower, L. E., Ditkowsky, S. P., Klien, B. A., and Bronstein, I. P.: Arteriovenous Angioma of Mandible and Retina With Pronounced Hematemesis and Epistaxis. Am. J. Dis. Child. **64**: 1023, 1942.

A case is reported of an arteriovenous angioma of the mandible and retina.

An obscure cause for spurious hematemesis and epistaxis may be a vascular lesion of the jaw with bleeding around the teeth.

AUTHORS.

Dill, L. V., and Isenhour, C. E.: Occurrence of Atheroma in the Aorta in Rabbits With Renal Hypertension. Arch. Path. 33: 655, 1942.

Atheromatous plaques were found in the aortas of rabits with persistent hypertension, produced by aortic constriction proximal to the origin of the renal arteries. The plaque formation seemed to be proportional to the elevation and duration of the hypertension. It was also seen more frequently in animals in which frequent pregnancies had occurred.

KERSHBAUM.

Peery, T. M.: Incomplete Rupture of the Aorta. Arch. Int. Med. 70: 689, 1942.

Small tears in the intima and media of the aorta are not uncommon findings at autopsy in cases of hypertension. These tears are thought to be an early stage of dissecting aneurysm, the stage before actual dissection has occurred. Most of the tears encountered have been transverse and across one of the commissures of the aortic valve. Tears in this area may result in slipping downward of the commissures so that the three valve cusps do not approximate, resulting in the clinical manifestations of aortic insufficiency. In some cases the tears heal at this stage, resulting in crippling of the aortic valve and death from congestive heart failure. In other cases dissection may occur days or months later, through the base of the old tear, and obliterate the evidence of a stage of incomplete rupture. In several instances reconstruction of the past history of a case of dissecting aneurysm has revealed two stages. The original period of substernal pain and sudden dyspnea or choking probably corresponds to the stage of actual dissection. If the tear occurs higher in the aorta, so that there is no effect upon the commissures, there may be no aortic insufficiency, and clinical manifestations may be slight. Occasionally a rough, rasping systolic murmur is noted over the aortic area. In cases in which dissection is preceded by incomplete rupture, the actual dissection is usually short, with termination by hemopericardium and cardiac tamponade. Of the eleven cases reported, five have shown incomplete aortic tears as purely incidental autopsy findings; two have died of congestive heart failure due to aortic insufficiency; and four have later developed dissecting aneurysm which resulted in death.

AUTHOR.

Bergman, A., and Neuman, J.: Thromboarteriosclerosis and Venous Thrombosis. Medicina, Buenos Aires 3: 87, 1942.

The clinical diagnosis of thromboarteriosclerosis does not presuppose the anatomical finding of an arterial thrombus or embolus.

The thromboses of the deep veins can aggravate the clinical picture of ischemia and lead to the amputation of a limb.

AUTHORS.

Ershler, I., Kossmann, C. E., and White, M. S.: Venous Pressure and Circulation Time During Acute Progressive Anoxia in Man. Am. J. Physiol. 138: 593, 1943.

In nineteen young, healthy, male subjects, acute progressive anoxia, induced by rebreathing, had the following effects:

The venous pressure showed a variable response. In four subjects it progressively decreased. In seven subjects, who fainted during the rebreathing, the venous pressure rose precipitously just before syncope, suggesting failure of the right ventricle. In all cases the venous pressure was restored promptly to normal by permitting the subject to breathe room air.

The circulation time from the right arm to the tongue was decreased in all subjects. This decrease was statistically significant. The rate of circulation was normal or slightly slower in some cases as soon as the oxygen saturation of the blood was restored to the control level.

AUTHORS.

Naide, M.: Treatment of Leg Ulcers With Blood and Concentrated Plasma. Am. J. M. Sc. **205**: 489, 1943.

A simple method has been described for the treatment of ischemic and varicose leg ulcers with patient's own blood and with concentrated plasma. Nine of fifteen ulcers, refractory to other treatment, were healed, two were improved, and four failed to heal. This treatment results in rapid relief of pain and subsidence of the local inflammatory reaction.

AUTHOR.

Weston, R. E., Janota, M., Levinson, S. O., and Necheles, H.: Studies on Hemoconcentration and Shock Following Severe Hemorrhage. Am. J. Physiol. **138**: 450, 1943.

Typical shock has been reproduced by graded hemorrhage in eleven nondehydrated, and in fifteen dehydrated, unanesthetized, normal dogs.

In two of the nondehydrated (18 per cent), and in eight of the dehydrated animals (53 per cent), hemoconcentration occurred. Plasma volume and plasma protein determinations, before and after hemorrhage, revealed that the animals which hemoconcentrated actually lost additional plasma fluid and protein as shock developed.

Pathologic changes consisting of gastrointestinal engorgement and hemorrhage, pulmonary congestion and engorgement, and occasional changes in other viscera were observed in a number of animals.

The hemodiluting, nondehydrated animals tolerated an average total blood loss of 49 per cent as compared to an average total blood loss of 43 per cent tolerated by the other animals.

The changes in plasma protein concentration after hemorrhage indicated that the hemoconcentrating dehydrated animals hemodiluted during and after hemorrhage to a lesser degree than the other three groups. This relative inability to hemodilute could explain their inability to tolerate as much bleeding before going into shock, and could lessen the masking by earlier hemodilution of the subsequent hemoconcentration as shock develops.

It is suggested that the conflicting reports as to the occurrence of hemoconcentration after hemorrhage may be related to the state of hydration of the animals studied.

It is concluded that there are no definite grounds for differentiating between hemorrhagic shock and shock from other causes.

AUTHORS.

Fox, T. T., Travell, J., and Molofsky, L.: Action of Digitalis on Conduction in the Syndrome of Short PR Interval and Prolonged QRS Complex. Arch. Int. Med. **71**: 206, 1943.

A case is reported in which the electrocardiographic picture of short P-R interval in association with prolongation of the QRS complex was exhibited. Observations were made over a period of nearly two years.

The effect of changes in vagal activity produced in various ways was studied.

The effect of atropine sulfate on this syndrome was always to shorten the QRS time. This indicates that there was a vagal component in the mechanism of the syndrome.

In repeated experiments digitalis uniformly produced widening of the abnormal QRS complex. That this effect involves vagal function was demonstrated by its disappearance after administration of atropine.

The results of this study are in harmony with the hypothesis that this syndrome is due to an aberrant conduction mechanism joining the sinal node with one of the ventricles. According to this hypothesis, the widening of the QRS complex by digitalis is due, not to an action of the drug on intraventricular conduction, but rather to depression of the auriculoventricular node, resulting in increased activity of the aberrant auricular conduction tissue with consequent increased asynchrony of the ventricular responses.

AUTHORS.

Erratum

Fig. 1 of the article by William Dressler, "Myocardial Infarction Indicated by an Electrocardiographic Pattern in Which T_1 is Lower Than T_3," page 314, September, 1943, issue of the JOURNAL, was printed upside down. It is reprinted below in its proper position.

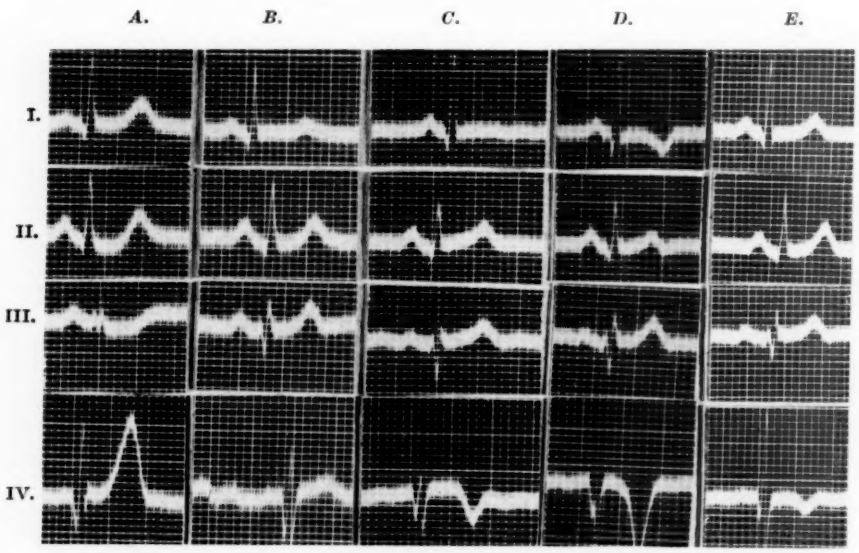

Fig. 1.—Case 1. *A*, Three hours after a severe anginal attack. The S-T segment is depressed in Leads II and III, and there is no corresponding elevation in Lead I. T_3 is nearly isoelectric. There is a deep Q wave and a high T wave in Lead IV.

B, Thirteen hours after the attack. The depression of the S-T segment in Leads II and III has subsided. T_1 has become flatter, and T_3 upright, resulting in the pattern $T_1<T_3$. A W-shaped QRS complex is visible in Lead IV, and T_4 is of low voltage.

C, Five days after the attack. The S-T segment in Lead I is slightly convex, and a dip has appeared at the end of T_1. There is sharp inversion of T_4.

D, Five weeks after the attack. T_1 is inverted and there is a marked increase in the voltage of the negative T_4.

E, Four and a half months after the attack. T_1 has become positive again. The inverted T_4 has decreased in voltage.

Book Reviews

ROENTGENOLOGY OF THE HEART: Prepared by Robert M. Daley, M.D., Richard S Gubner, M.D., and Harry E. Ungerleider, M.D., for the Medical Department of the Equitable Life Assurance Society of the United States. Published by the Picker X-Ray Corporation for free distribution, 1943, 19 pages, many illustrations.

This brochure deals with techniques for measurement of heart size and interpretation of the teleoroentgenogram, points out the practical applications of the kymogram, outlines the criteria for enlargement of the various heart chambers, and presents in very clear and concise fashion the significance of cardiac enlargement in the common types of heart disease. A bibliography of the more important contributions to the subject of cardiac roentgenology is appended.

For the most part, the material presented represents the consensus of investigators in this field. It contains a few statements concerning which one might hold an honest difference of opinion, depending upon one's training and experience. For example, on page 4, the authors recommend three views in the routine roentgenographic study of the cardiovascular shadow, the posteroanterior and the two obliques. In the experience of the reviewer, the lateral view should be included routinely, and usually either the left or right anterior oblique is sufficient in any given case, depending upon the type of cardiac disease which is present. In persons of middle age or beyond, the left anterior oblique view is desirable for visualizing the entire thoracic aorta, whereas, in children and young adults, the right anterior oblique view is the more important because of the likelihood of mitral valve disease and congenital lesions. The authors are to be commended for encouraging the use of the midclavicular line rather than the nipple line as a reference for the location of the apex impulse, but it should be pointed out that "the leftmost point at which a definite forward impulse is imparted to the palpating finger" is not as accurate as the point of maximum impulse for locating the actual cardiac apex. Extensive studies in which the heart borders have been projected orthodiascopically to the anterior chest wall have shown that the point of maximum impulse corresponds much more closely to the anatomic apex. The statement that "The electrocardiogram is the most sensitive method to detect left ventricular hypertrophy" is open to question. In the experience of the reviewer, the electrocardiographic pattern commonly known as "left ventricular strain" (Barnes) is likely to be a late manifestation, and frequently does not appear until long after ventricular enlargement is demonstrable by roentgenologic examination. It is true, however, that in the occasional case of so-called "concentric hypertrophy," the electrocardiographic pattern may be characteristic when no enlargement can be detected by measurement of the cardiac shadow.

Under the heading "Interpretation of the Teleoroentgenogram," the brochure calls attention to some very important points that are not generally recognized. For example, marked changes in the size of the heart shadow in a given person may result from deep inspiration or forced expiration, and only a teleoroentgenogram taken with the breath suspended in ordinary inspiration is suitable for heart size measurements. The pitfalls presented by the extrapericardial fat pad, the funnel chest, and scoliosis of the thoracic spine are well illustrated. Routine fluoroscopic examination, particularly in the lateral and oblique positions, tends to minimize the errors resulting from these complications.

In the opinion of the reviewer, the section on mensuration contains a really valuable contribution, namely, a relatively simple method of estimating the frontal area from measurements of the long and broad diameters, which was originally published by Ungerleider and Gubner in the AMERICAN HEART JOURNAL for October, 1942. Most cardiologists will admit, as emphasized by Ungerleider, that the cardiothoracic ratio is the poorest roentgenographic method of detecting cardiac enlargement, whereas orthodiascopic measurement of the frontal area of the cardiac silhouette is probably the most accurate. The latter has the obvious disadvantage of requiring a considerable amount of training in the technique. A teleoroentgenogram, on the other hand, can be taken in any laboratory by an ordinary technician. If the other disadvantages of measuring the frontal area, namely, the completing of the upper and lower borders and the use of a planimeter, could be obviated, one would have an ideal method for even the untrained. The method proposed by Ungerleider and Gubner approaches this ideal. They have shown that, by measuring the long and broad diameters of the frontal cardiac shadow and applying the formula for the area of an ellipse, the frontal area of the heart can be closely approximated without actually resorting to planimetry. This will be particularly welcome news to those who have found it impossible to obtain a planimeter because of war restrictions. The authors have constructed a nomogram from which the actual area can be estimated by simply laying a ruler across two scales and reading the frontal area on a third scale. The reviewer has applied this method to 155 of his own orthodiagrams in which the area had been measured by a planimeter. This group was made up of patients of all ages, and included normal hearts as well as the common types of heart disease in various stages. The calculated area corresponded exactly to the planimetric determination in 20 subjects (13 per cent), was slightly greater in 81 (52 per cent) and smaller in 54 (35 per cent). The calculated area exceeded the measured area by more than 5 per cent in 7 per cent of the cases, and dropped below minus 5 per cent in 2 per cent of the entire group. Using the measured area as a basis, the average amount by which the calculated area exceeded the planimetric area in the 81 cases was plus 3 per cent, and the average of the 54 cases which fell below the measured area was minus 2.5 per cent. This relatively close approximation to the planimetric area indicates that the method has a practical application of distinct value in the great majority of cases. The normal range probably should be increased by about 3 per cent to allow for the slightly decreased accuracy of the ellipsoid formula.

On page 9 of the brochure, the authors state that the broad diameter is *sometimes* drawn as the sum of two perpendiculars from the long diameter to the right and to the left heart borders. In the reviewer's experience, only the vertically placed heart permits the broad diameter to be drawn in one continuous line, and in *most* instances it has to be divided. Variation in the placing of the portion of the broad diameter which lies between the long diameter and the left border results in considerable difference in the calculated area. By trying several different points it was found that drawing it from the lower end of the left auricular salient (approximately 1.5 to 2 cm. below the junction of the left cardiac border and pulmonic arch) gave the most consistent results. The teleoroentgenogram illustrated in the brochure represents an ideal, but not the most common, type of cardiac silhouette. The nomogram is highly accurate, but would be much easier to use if the long and broad diameter scales were divided at every 0.2 cm. instead of every 0.5 cm. Its usefulness could be further enhanced by extending the frontal area scale in both directions.

The other methods listed for estimating heart size are probably of rather dubious value from a practical standpoint, and considerably less accurate than the method of Ungerleider and Gubner. What the authors refer to as the "aortic arch diameter" (sum of maximum extensions to the right and left borders of the vascular

pedicle from midline), on page 9, in reality represents the width of the great vessels, including the superior vena cava as well as the aorta. A more accurate method of measuring the diameter of the aortic arch is shown on page 10.

The criteria for the enlargement of the cardiac chambers are well presented. However, it should be emphasized that there is no accurate means of detecting enlargement of the right ventricle except by angiocardiography. The roentgenograms illustrating the changes in size and shape of the heart in various common types of heart disease are characteristic of the conditions represented.

On the whole, the brochure is well done, the material is authentic, and the illustrations have been carefully selected. It properly emphasizes the fact that measurement of cardiac enlargement has been lifted out of the realm of guesswork and has been made a procedure of mathematical precision. A simplified modification of the frontal area method of measuring heart size is presented, together with a nomogram for estimating the frontal area and a percentage deviation table which obviate the necessity for all computations. In the reviewer's limited experience with this "short cut," it is not quite as accurate as the planimeter, but, nevertheless, is highly practical.

CHESTER M. KURTZ.

HYPERTENSION: A MANUAL FOR PATIENTS WITH HIGH BLOOD PRESSURE: By Irvine H. Page, M.D., Director, Lilly Clinic, Indianapolis City Hospital. Charles C Thomas, Springfield, Ill., 1943, 69 pages, plus index, 7 illustrations, $1.50.

The author, who is noted for his researches in the field of hypertension, has written a manual for laymen on the subject of hypertension. He has "attempted to give the patient an insight into his illness that he may be spared some of the dismay and alarm and avoid quackery that will assail him from every side." The author has "tried to explain" the purpose of various examinations given to persons with high blood pressure, what hypertension is, and what can be done about it. He has been eminently successful. That some of the explanations are somewhat complex for laymen does not detract from the value of the book; most of them are clear and precise. Perhaps the author could have condemned many proprietary remedies with advantage, but that would have made many patients unhappy with the treatment which they are receiving; the placebo effects of otherwise useless proprietary remedies may be substantial. The book is valuable not only for laymen for whom it was written, but for physicians for whom it was not written; many of them still maintain beliefs in old and scientifically disproved theories which are efficiently discarded in this volume. Almost all patients with hypertension and almost all doctors who treat patients with hypertension would benefit greatly from reading this manual. The book is highly recommended. In general it is a clear explanation of a puzzling and common disease which constitutes one of the greatest problems of modern life.

E. V. ALLEN.

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